METHIDATHION
(SUPRACIDE)

RISK CHARACTERIZATION DOCUMENT

REVISION 1

DRAFT

Medical Toxicology Branch

DEPARTMENT OF PESTICIDE REGULATION

CALIFORNIA ENVIRONMENTAL PROTECTION AGENCY

August 4, 2005

Contributors and Acknowledgments

Principal Author:	Carolyn M. Lewis, M.S., D.A.B.T. Associate Toxicologist Health Assessment Section Medical Toxicology Branch
Toxicology Reviews:	Marilyn H. Silva, Ph.D., D.A.B.T. Staff Toxicologist SB 950 Data Review Section Medical Toxicology Branch
Dietary Exposure Assessment:	Carolyn M. Lewis, M.S., D.A.B.T. Associate Toxicologist Health Assessment Section Medical Toxicology Branch
	Wesley C. Carr, Jr., M.S. Associate Pesticide Review Scientist Health Assessment Section Medical Toxicology Branch
Occupational and Ambient Air Exposure Assessment:	Sheryl Beauvais, Ph.D. Staff Toxicologist Worker Health and Safety Branch
Peer Reviewed By:	Nu-may R Reed, Ph.D., D.A.B.T. Staff Toxicologist Health Assessment Section Medical Toxicology Section
	Keith F. Pfeifer, Ph.D., D.A.B.T. Senior Toxicologist Health Assessment Section Medical Toxicology Branch
	Jay P. Schreider, Ph.D. Primary State Toxicologist Medical Toxicology Branch

DPR acknowledges the review of this document by the Pesticide Epidemiology Unit, Office of Environmental Health Hazard Assessment.

TABLE OF CONTENTS

METHIDATHION

SUMMARY

Methidathion (O,O-dimethyl-phosphorodithioate, S-ester with 4-(mercaptomethyl)-2-methoxy-Δ-1,3,4-thiadiazolin-5-one) was first registered in 1974 by Ciba Geigy Corporation (U.S. EPA, 1989). The Department of Pesticide Regulation (DPR) in the California Environmental Protection Agency placed methidathion on the high-priority list for risk assessment based on possible adverse effects identified in chronic toxicity, oncogenicity and chromosomal aberrations studies submitted under the Birth Defect Prevention Act (SB 950). In 1989, the California Assembly passed AB2161 which requires DPR to conduct dietary risk assessments for all pesticides with food crop uses. The Department of Pesticide Regulation (DPR) in the California Environmental Protection Agency completed a Risk Characterization Document (RCD) for methidathion in 2001 that addressed dietary and drinking water exposure. No mitigation was needed for either dietary or drinking water exposure; however, an acute tolerance assessment suggested that the tolerances for citrus fruit and apples should be reduced to be health protective. The purpose of this revision to the Risk Characterization Document for methidathion is to add the occupational and ambient air exposure to dietary and drinking water exposure, evaluating them separately and in combination.

Toxicity

Methidathion and its oxygen analog produce their toxic reaction primarily through their inhibition of cholinesterase (ChE) enzymes, including acetylcholinesterase (AChE). AChE is responsible for the termination of nerve impulses across synaptic clefts of certain types of nerves in the central and peripheral nervous systems. The effects observed in laboratory animals after acute exposure to methidathion were various neurological signs typical of ChE inhibitors, including ataxia, muscle fasciculations, convulsions, excessive salivation and lacrimation, difficulty in breathing and death. The most thorough evaluation of the acute neurotoxic effects was in an acute neurotoxicity study where methidathion was administered by oral gavage to rats. The study was selected as the definitive study for evaluating the acute dietary, drinking water, occupational and ambient air exposure to methidathion. The acute No-Observed-Effect Level (NOEL) from this study was estimated to be 0.3 mg/kg based on a significant reduction of ChE activity in the cerebral cortex of male rats.

Brain ChE inhibition and cholinergic signs similar to those observed with acute exposure were also observed in laboratory animals after subchronic exposure. In addition, reduced body temperatures, reduced body weights and food consumption, hematological changes suggestive of anemia, changes in serum enzyme levels suggestive of liver toxicity, and lesions in the liver, gallbladder, stomach, kidney and heart were seen. The lowest subchronic NOEL was 0.2 mg/kg/day that was observed in a 90-day neurotoxicity study in rats based reduced ChE activity in RBCs and various brain regions in both sexes. Dietary and drinking water exposure to methidathion did not vary significantly with season; however, seasonal occupational and ambient air exposure to methidathion is anticipated. Therefore, the subchronic neurotoxicity study in rats was selected as the definitive study for evaluating seasonal occupational and ambient air exposure to methidathion.

Several developmental and reproductive effects were seen in studies including reduced pup weights, signs of maternal neglect, and reduced maternal index. The NOELs for fetal or pup effects were equal to or higher than the maternal or parental NOELs, suggesting there is no increased pre- or post-natal sensitivity to methidathion. However, in one study where the LD_{50} was determined in both weanling and adult rats, the weanling rats appear to be slightly more sensitive.

The effects observed in laboratory animals with chronic exposure to methidathion were similar to those observed with subchronic exposure, except that evidence of hepatotoxicity was more common. Although both the neurotoxicity and hepatoxicity were seen in most species, there appeared to be some species differences in the pharmacokinetics of methidathion. Cholinesterase inhibition appeared to be the more sensitive endpoint in rats while the hepatotoxicity was a more sensitive endpoint in dogs. The lowest NOEL in a chronic study of acceptable quality was 0.15 mg/kg/day based on elevated liver enzymes in the serum and microscopic lesions in the liver of dogs exposed to methidathion in the diet for 1 year.

An increase in liver tumors was also observed in male mice in two different carcinogenicity studies. The tumors were only observed at dose levels that produced significant increases in other non-neoplastic lesions in the livers of mice suggesting that they maybe secondary to these non-neoplastic lesions. However, direct DNA interaction could not be eliminated based on a few positive genetic toxicity tests. Therefore, it was assumed that a non-threshold mechanism was involved and the carcinogenic potential of methidathion was evaluated using a linear approach based on the increase in liver tumors in male mice. The cancer potency was estimated to range from 0.34 $(mg/kg/day)^{-1}$ for the maximum likelihood estimate to 0.53 $(mg/kg/day)^{-1}$ for the 95% upper bound estimate.

Exposure

Dietary

A tiered approach was used in the dietary exposure analysis. Initially, only DPR monitoring data from 1992-1995 were used. Further refinements were added as needed, including 1) use of PDP monitoring data for commodities that contributed significantly to exposure, 2) adjustment for percent crop treated, and 3) elimination of residues from animal products. Dietary consumption of commodities with methidathion residues by various population subgroups was based on USDA Continuing Survey of Food Intakes by Individuals (CSFII) from 1989 to 1992. The estimated acute dietary exposure dosages ranged from 253 to 1,068 ng/kg using only DPR monitoring data. The population subgroup with the highest acute dietary exposure was nursing infants less than 1 year old. The estimated chronic dietary exposure dosages ranged from 2 to 10 ng/kg/day with use of PDP data, adjustment for percent crop treated and the elimination of residues on animals products. Non-nursing infants less than 1 year old had the highest estimated chronic dietary exposure.

Drinking Water

No methidathion residues have been detected in well water monitored by DPR; however, they have been detected in surface water in California. Drinking water exposure dosages were based on DPR and U.S. Geological Survey monitoring data of surface water in California. The estimated acute drinking water exposure to methidathion ranged from 29 to 181 ng/kg. Non-nursing infants had the highest estimated acute exposure to methidathion in drinking water. The estimated chronic drinking water exposure ranged from 1 to 4 ng/kg/day. Non-nursing infants also had the highest estimated chronic exposure to methidathion in drinking water.

When dietary and drinking water exposure to methidathion were combined, the acute exposure ranged from 273 to 1,067 ng/kg. Children 1 to 6 years old had the highest combined acute exposure. The combined chronic exposure to methidathion ranged from 2 to 14 ng/kg/day. Non-nursing infants had the highest combined chronic exposure to methidathion.

Occupational

There were no acceptable chemical-specific occupational exposure studies for methidathion, so handler exposure was estimated using the Pesticide Handler Exposure Database (PHED). Daily, seasonal, chronic and lifetime exposure dosages were estimated for 9 handler exposure scenarios. The Absorbed Daily Dosage (ADD) represented the upper confidence limit on the 95th percentile after adjusting for dermal and inhalation absorption using default values of 50 and 100%, respectively. The ADDs for handlers ranged from 0.0034 to 5.85 mg/kg/day. The Seasonal Average Daily Dosage (SADD) was the upper confidence limit on the mean daily exposure during the high-end use months. The high-end use months ranged from 1 to 2 months for handlers. The SADDs for handlers ranged from 0.044 to 1.55 mg/kg/day. The Annual Average Daily Dosage (AADD) was calculated by multiplying the SADD by the annual use months per year and dividing by 12 months. The AADDs for handlers ranged from 0.007 to 0.243 mg/kg/day. The Lifetime Average Daily Dosage (LADD) was estimated by multiplying the AADD by 40 years of work in a lifetime and dividing by 75 years in a lifetime. The LADDs for handlers ranged from 0.004 to 0.130 mg/kg/day. Mixer/loader/applicators (M/L/As) using low-pressure handwands had the lowest acute exposure dosages while airblast and aerial applicators had the highest acute exposure dosages. The M/L/As using backpack sprayers and low-pressure handwands were not considered to have seasonal and chronic exposures, so the lowest seasonal and chronic exposures among handlers were for groundboom applicators. Aerial and airblast applicators continued to have the highest seasonal and chronic exposures.

The exposure dosages were calculated for 3 field worker exposure scenarios using dislodgeable foliar residues (DFRs) and transfer factors (TFs). The DFRs for the ADDs and SADDs were those anticipated at the end of the re-entry interval (REI) and REI plus 3 days, respectively, for most activities. The default dermal absorption of 50% was applied to the field worker exposure calculations. The ADDs for field workers ranged from 0.0026 to 0.119 mg/kg/day. The SADDs for field workers were between 0.0014 and 0.0214 mg/kg/day. The annual use months for field workers ranged from 3 and 5 months. The AADDs ranged from 0.0006 to 0.0053 mg/kg/day for field workers. The LADDs were between 0.0003 and 0.0028 mg/kg/day for field workers.

Ambient Air

Application site and ambient air was monitored in Tulare County during June and July of 1991. Tulare County had the highest use of methidathion in 1991, primarily in June and July. The acute exposure estimates (i.e., ADDs) for application site air were 519 and 264 ng/kg for adults and children, respectively, using the 95th tolerance limits percentile and the default inhalation absorption of 100%. The ADDs for ambient air were initially calculated for the Jefferson Elementary School in Lindsay since it was the only site with one or more samples above the limit of quantitation. The ADDs for ambient air at the Jefferson site ranged from 185 ng/kg for adults to 389 ng/kg for children. The SADDs for ambient air at the Jefferson site ranged from 22 ng/kg/day for adults to 47 ng/kg/day for children based on the average air concentration during the monitoring period. The AADDs for ambient air at the Jefferson site ranged from 17 ng/kg/day for adults to 35 ng/kg/day for children, assuming the season of potential exposure is 9 months per year. Due to their higher respiratory rate relative to their body weight, children consistently had the highest exposure.

Risk Characterization

The risk for non-carcinogenic health effects is expressed as a margin of exposure (MOE) which is the ratio of the NOEL from the animal study to the human exposure dosage. Generally, an MOE of at least 100 is desirable assuming that humans are 10 times more sensitive than animals and that there is a 10-fold variation in the sensitivity between the lower distribution of the overall human population and the sensitive subgroup. The negligible carcinogenic risk level is generally considered 1 excess cancer case in a million.

Dietary

The MOEs for acute dietary exposure to methidathion in the various population subgroups ranged from 280 to 1,200. The MOEs for chronic dietary exposure ranged from 15,000 to 96,000. The estimated carcinogenic risk from dietary exposure to methidathion ranged from 0.9 to 1.5 excess cancers in a million people.

Drinking Water

The MOEs for acute drinking water exposure to methidathion ranged from 1,700 to 10,000. The MOEs from chronic drinking water exposure ranged from 38,000 to 230,000. The estimated carcinogenic risk from drinking water exposure to methidathion ranged from 0.3 to 0.5 excess cancers in a million people.

The MOEs for combined acute dietary and drinking water exposure to methidathion ranged from 280 to 1,100. The MOEs for combined chronic exposure ranged from 11,000 to 68,000. The estimated carcinogenic risk from combined dietary and drinking water exposure to methidathion ranged from 1.2 to 1.9 excess cancer cases in a million people.

Occupational

The MOEs for acute, seasonal and chronic occupational exposure to methidathion was less than 100 for all exposure scenarios, except for harvesting and thinning of citrus. The MOEs were less than 10 for most exposure scenarios and less than 1 for some scenarios (aerial handlers and airblast applicators). The carcinogenic risk estimates for occupational exposure to methidathion all exceeded the negligible risk level. The estimated carcinogenic risk based on the maximum likelihood estimate ranged from 10^{-2} to 10^{-4}. The upper bound estimate of carcinogenic risk was between 10^{-1} and 10^{-4}. Airblast applicators had the highest estimated carcinogenic risk.

Ambient Air

The MOEs for acute exposure to methidathion in application site air were greater than 500 for both children and adults. The MOEs for acute, seasonal and chronic exposure to methidathion in ambient air were greater than 500 for both children and adults. These MOEs are sufficiently high to not require mitigation, but some are low enough to meet the criteria for identifying methidathion as a toxic air contaminant. The carcinogenic risk estimates for the general public based on the ambient air exposure ranged from 6 to 9 x 10^{-6} which is above the negligible risk level of 10^{-6}. This carcinogenic risk level also meets the criteria for identifying methidathion as a toxic air contaminant since the exposure levels are not 10-fold below the negligible carcinogenic risk level. Since this carcinogenic risk level for ambient air is above the negligible risk level mitigation may be needed.

Aggregate

Aggregate exposure for agricultural workers and the general public were evaluated. The MOEs for most agricultural workers were already significantly less than 100 from occupational exposure alone without adding in additional exposure from diet, drinking water and ambient air. Therefore, the aggregate MOEs for most agricultural workers was not significantly lower than their occupational MOEs. The aggregate MOEs for the general public were adequate for all exposure durations; however, the aggregate carcinogenic risk estimates exceeded the negligible risk level. The ambient air exposure appears to be the primary contributor since the carcinogenic risk estimates from ambient air exposure alone clearly exceeded the negligible risk level. Dietary exposure was also a significant contributor to the aggregate carcinogenic risk for the general public since the carcinogenic risk estimates from dietary exposure alone were also slightly greater than the negligible risk level. The contribution of drinking water exposure to the aggregate carcinogenic risk appears to be the least significant since the carcinogenic risk estimates for drinking water exposure alone were slightly less than the negligible risk level.

Tolerance Assessment

A tolerance assessment for methidathion was conducted assuming commodities were consumed at their tolerance level for acute exposure. The MOEs for potential acute effects were less than 100 for one or more population subgroups for citrus fruit and apples. Based on these estimates, the tolerances for these commodities, especially citrus fruit, should be reviewed.

Reference Concentrations

Ambient air concentrations of methidathion below the reference concentration (RfC) are considered sufficiently low to protect human health. The acute (24-hour) RfC for methidathion was 5.1 $\mu g/m^3$ (0.41 ppb) based on the reduced ChE activity in the cerebral cortex of male rats. The seasonal RfC was 3.4 $\mu g/m^3$ (0.27 ppb) based on reduced ChE activity in the RBCs and various brain regions of rats. The chronic RfC for methidathion was 2.5 $\mu g/m^3$ (0.21 ppb) based elevated liver enzymes in the serum and histological lesions in the liver of dogs. The air concentration below which there is no regulatory concern about carcinogenic effects is 68 ng/m^3 (5.5 ppt).

I. INTRODUCTION

A. REGULATORY BACKGROUND

Methidathion (O,O-dimethyl-phosphorodithioate, S-ester with 4-(mercaptomethyl)-2-methoxy-Δ-1,3,4-thiadiazolin-5-one) was first registered in 1974 by Ciba Geigy Corporation (U.S. EPA, 1989). The Department of Pesticide Regulation (DPR) in the California Environmental Protection Agency placed methidathion on the high-priority list for risk assessment based on possible adverse effects identified in chronic toxicity, oncogenicity and chromosomal aberrations studies submitted under the Birth Defect Prevention Act (SB 950). Methidathion is also a high-priority pesticide for risk assessment under the California Toxic Air Contaminant Act (AB 1807). In 1989, the California Assembly passed AB2161 which requires DPR to conduct dietary risk assessments for all pesticides with food crop uses.

Methidathion was placed in reevaluation in 1989 along with chlorpyrifos, diazinon, and ethyl parathion which were used as dormant sprays to control scale and other pests on almond trees (DPR, 1996a). Reevaluation of these organophosphates was based on a study conducted by the California Department of Fish and Game (CDFG) which identified possible adverse effects in resident and migratory red-tailed hawks. The registrants were then asked to submit additional data to further evaluate this potential wildlife problem. During the course of these field studies, the use of ethyl parathion as a dormant spray was canceled. Field and laboratory studies indicated that methidathion had the greatest effect on cholinesterase inhibition of these four organophosphate pesticides with the exception of ethyl parathion. The principle route of exposure to these chemicals for raptors appears to be the dermal route from perching on sprayed trees. DPR concluded that no mitigation was needed because the elimination of ethyl parathion resulted in a significant reduction in the raptors identified with lowered cholinesterase levels and, therefore, continued use of the other three organophosphates did not pose a significant hazard. CDFG concurred with DPR's decision.

In 2001, DPR completed a Risk Characterization Document (RCD) for methidathion addressing dietary and drinking water exposure. No mitigation was needed for either the dietary or drinking water exposure, although the tolerance assessment suggested that the tolerances for citrus fruit and apples should be reduced to be health protective. This document has been revised to include additional occupational and ambient air exposure assessments for methidathion. DPR is also updating its use of ChE inhibition data in the risk assessment for ChE inhibitors. In anticipation of changes in the use of these endpoints in the risk assessments, NOELs for both blood and brain ChE inhibition were included in this document.

B. CHEMICAL IDENTIFICATION

Methidathion is an organophosphate insecticide and acaricide (U.S. EPA, 1988). Methidathion and its oxygen analog produce their toxic reaction primarily through their inhibition of cholinesterase (ChE) enzymes, including acetylcholinesterase (AChE) and butyryl-cholinesterase (BuChE). AChE is also called specific or true cholinesterase and is found near cholinergic synapses, in some organs (e.g., lung, spleen, gray matter) and in hematopoietic cells

(Lefkowitz *et al.*, 1990). Normally, AChE metabolizes acetylcholine to acetate and choline, which results in the termination of stimulation to dendritic nerve endings and motor endplates. Acetylcholine is the neurochemical transmitter at endings of postganglionic parasympathetic nerve fibers, somatic motor nerves to skeletal muscle, preganglionic fibers of both parasympathetic and sympathetic nerves, and certain synapses in the central nervous system (Murphy, 1986). The concentration at which methidathion inhibited 50% of the free AChE activity in electric eel and bovine red blood cells (RBCs) was reported to be 2.3×10^{-4} M and 4.6×10^{-4} M, respectively, compared to paraoxon which was 2.8×10^{-7} M and 9.6×10^{-8} M, respectively (Mionetto *et al.*, 1992). The bimolecular rate constant, Ka ($M^{-1}mm^{-1}$), of methidathion was 1.9×10^{2} and 9.3×10^{1} for the free AChE in electric eel and bovine RBCs, respectively, compared to paraoxon which was 4×10^{5} and 0.7×10^{6}. However, the active metabolite of methidathion, the oxygen analog, was not used, so the ability of methidathion to inhibit AChE was underestimated in this experiment.

The inhibition of AChE results in the accumulation of endogenous acetylcholine in nerve tissue and effector organs. In acutely toxic episodes, muscarinic, nicotinic and central nervous system (CNS) receptors are stimulated with characteristic signs and symptoms occurring throughout the peripheral and central nervous systems (Ellenhorn and Barceloux, 1988; Murphy, 1986). Muscarinic effects can include increased intestinal motility, bronchial constriction and increased bronchial secretions, bladder contraction, miosis, secretory gland stimulation and bradycardia. Nicotinic effects include muscle weakness, twitching, cramps and general fasciculations. Accumulation of acetylcholine in the CNS can cause headache, restlessness, insomnia, anxiety and other non-specific symptoms. Severe poisoning results in slurred speech, tremors, ataxia, convulsions, depression of respiratory and circulatory centers and, eventually, coma.

Butyrylcholinesterase (BuChE), sometimes referred to as plasma ChE, pseudo-cholinesterase, or serum esterase, is also inhibited by methidathion. Any reference in this document to "cholinesterase", without specifically indicating that the enzyme is serum or plasma ChE, should be interpreted as AChE. BuChE only occurs to a limited extent in neuronal elements of the central and peripheral nervous systems in adults, but there is compelling evidence for a role of BuChE in the developing nervous system and in the co-regulation of acetylcholine (ACh) levels in the mature nervous system. The evidence for a role in the co-regulation of ACh is based on 1) substrate inhibition of AChE, but not BuChE, at high concentrations of ACh, 2) survival of AChE knockout ($AChE^{-/-}$) mice past birth, 3) an increase in BuChE levels in Alzheimer's patients while the AChE levels decrease (Giacobini, 2003; Li *et al.*, 2000; Ballard and Perry, 2003). Unlike AChE, BuChE occurs primarily in non-neuronal or non-synaptic sites in adults like the liver, lung, and plasma and has no known physiological function (Lefkowitz *et al.*, 1990; Brimijoin, 1992; U.S. EPA, 1993; Pantuck, 1993). An atypical genetic variant of plasma cholinesterase has been associated with an increased susceptibility to various drugs, such as succinylcholine and cocaine (Lockridge, 1990; Pantuck, 1993). However, it is unclear if this increased susceptibility to certain drugs in people with the atypical plasma ChE translates to a possible adverse effect when plasma ChE is inhibited by organophosphates. There is some evidence suggesting that BuChE does play a role in the metabolism of organophosphates in that administration of exogenous BuChE provided significant protection against organophosphate toxicity in several species tested including rats, mice, guinea pigs and non-human primates (Raveh et al., 1997; Allon et al., 1998).

The physiological role of AChE in RBCs is also unknown. Due to the expression of AChE in several types of hematopoietic cell lines, it has been proposed that circulating AChE may be important in erythropoiesis (Grisaru *et al.* 1999). U.S. EPA does not consider RBC ChE inhibition an adverse effect in itself, but does use RBC ChE inhibition as a surrogate for peripheral ChE inhibition which is usually not measured (U.S. EPA, 2000a). Caution is needed when using RBC ChE as a surrogate since unlike nervous tissue, RBCs lack the ability to synthesize new AChE (Brimijoin, 1992). Consequently, the recovery of RBC ChE activity is much slower than in the central and peripheral nervous system because it is dependent on the replacement of RBCs.

C. TECHNICAL AND PRODUCT FORMULATION

Currently, there are three products registered for use in California containing methidathion: Supracide® 25W, Supracide® 2E and Supracide® 2E Liquipac. Supracide® 25W is a wettable powder containing 25% methidathion. Supracide® 2E and Supracide® 2E Liquipac are emulsifiable concentrates containing 24.4% methidathion with different packaging. The registrant for all three products is Gowan Company.

D. USAGE

Supracide® 25 W and 2E may be applied directly to the soil by injection, shank or chisel. It may also be applied as a spray by ground or aerial application. The application rate for most tree crops was 4 to12 lbs. of product (1 to 3 lbs. methidathion) per acre per application, except for citrus fruit which may be applied up to 20 per acre. For deciduous fruit and nut trees, the product is usually applied as a dormant spray and diluted in a minimum of 20 and 50 gallons of water per acre for aerial and ground application, respectively. For citrus and olives, the product is diluted in a minimum of 20 and 400 gallons of water per acre, respectively. Generally, only one application per season is made to deciduous fruit and nut trees and nursery stock. Up to 2 applications per season may be permitted with citrus at anytime, except during the bloom period or 2 weeks before harvest. Application rates for row and field crops ranged from 2 to 4 lbs. of product (0.5 to 1 lbs. methidathion) per acre per application. Three to 8 applications maybe applied to artichokes and safflower, respectively. The pre-harvest intervals (PHIs) ranged from 7 days for walnuts to 80 days for almonds. Applications to artichokes and almonds are prohibited after bud formation.

The use of methidathion has been decreasing since 1998 in which 178,451 lbs of methidathion were used in California. In 2003 (the most recent year use data is available), only 54,398 lbs of methidathion were used in California. The biggest degree was seen between 1999 and 2000 when use decreased by 45% primarily due to decreased use on almond and citrus trees. Despite these reductions, 85% of the total use for methidathion in 2003 was still on tree crops. Use on nut trees, citrus trees, stone fruit trees, olive trees and pome fruit trees represented 28%, 28%, 22%, 5% and 2% of the total, respectively.

E. ILLNESS REPORTS

Dermatitis was associated with exposure to organophosphate insecticides in 202 patients in Japan either as a solitary compound or as multiple compounds (Matsushita *et al.*, 1985). None of the cases of dermatitis associated with a solitary compound involved methidathion. In another study, 84 tea growers in Japan were given a patch test for 11 pesticides including methidathion (Fujita, 1985). Thirteen percent (4 males and 7 females) had an unequivocal positive response for methidathion and another 23% (4 males and 15 females) had an equivocal response. Five female tea growers had contact dermatitis from occupational exposure, one of which had a positive patch test for methidathion.

Eleven greenhouse applicators in Hungary were examined for potential health effects on two occasions approximately three months apart (Desi *et al.*, 1986). These workers were exposed to a variety of pesticides including methidathion. The examination included urinalysis, hematology, immunoglobulin levels, whole blood ChE activity, serum γ-glutamyl transferase activity, lymphocyte chromosome aberrations, and electrocardiography. No differences in these measurements were seen, except a slight increase (2.7%) in the numerical chromosome aberrations rate which was within the reported normal range (4-7%) for the Hungarian population.

The lymphocytes of 55 male agricultural workers from Hungry were examined for chromosome aberrations (Nehéz *et al.*, 1988). These men worked with a variety of pesticides including methidathion. Plasma cholinesterase activity was normal in all workers. Chromosome aberrations were not observed in any of the 41 men working in closed spaces (green houses or plastic tents), but there was a significant increase in chromosome aberrations in 14 men working in open fields. The investigators suggested that the increased chromosome aberrations in men working in open fields may be due to exposure to larger volumes of pesticides and/or to a contaminant in the products.

In a prospective cohort study, 204 farmers in Indonesia were evaluated for pesticide exposure and signs and symptoms (Kishi *et al.*, 1995). Methidathion was one of many pesticides used by these farmers. Extensive exposure to pesticides was seen because protective clothing was too hot or costly, resulting in a significantly higher incidence of signs and symptoms during the spraying season. Twenty-one percent of the respondents had 3 or more neurological, intestinal or respiratory signs or symptoms per spray operation. There was a dose-response relationship between the use of multiple organophosphates and the neurobehavioral signs and symptoms.

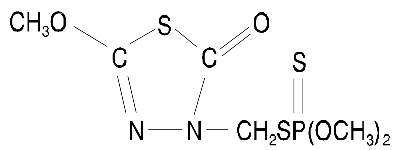
Five case reports of individuals poisoned with methidathion were available. A 25-year-old farmer ingested an unknown quantity of a 40% methidathion formulation (Teitelman *et al.*, 1975). At admission to the hospital, he was semicomatose, sweating, miotic, and had rales. The serum cholinesterase activity was zero a few hours after admission. He was treated with gastric lavage, atropine, obidoxime chloride, and cortisol hemisuccinate. He later developed jaundice, a high fever and went into a deep coma. After the first week, there was a gradual improvement. He was reevaluated at 2 months and no abnormalities were found, including any evidence of delayed neurotoxicity.

A 50-year-old Italian man ingested 20 ml of 20% methidathion formulation in a suicide attempt (Zoppellari *et al.*, 1990). He exhibited lacrimation, salivation, sweating, miosis, bradycardia, muscle fasciculations and mental confusion. He was treated with hemoperfusion, gastric lavage, atropine and pralidoxime. The clinical course appeared to vary as methidathion was redistributed from the fat to the blood. Methidathion was present in plasma, urine and gastric juice until the 6th, 7th and 8th day, respectively. Significant plasma and red blood cell (RBC) ChE inhibition was seen through day 8. There was no evidence of delayed neuropathy or NTE inhibition in the lymphocytes. He was fully recovered 45 days after exposure.

Three cases of methidathion poisoning in Crete were reported involving either intentional or accidental ingestion (Tsatsakis *et al.*, 1996). A 47-year old man developed miosis, sialorrhea, cyanosis and diffuse rales initially after ingesting 250 ml of a methidathion formulation (concentration not reported). His recovery was protracted and complicated by tonicoclonic spasms, fasciculations, atelectasis and arrhythmias despite treatment with gastric lavage, activated carbon, atropine and pralidoxime. The patient was fully recovered 45 days after exposure. A 74-year-old man did not recover after ingesting an unknown quantity of a 40% methidathion emulsifiable concentrate formulation. He had acute respiratory failure and was comatose on admission to the hospital. Despite treatment with atropine and pralidoxime, he developed pseudomonas sepsis and multiple organ failure. Progressively diffuse pulmonary fibrosis was the main cause of death. Another 70-year-old man died after ingesting 200 ml of a 40% methidathion emulsifiable concentrate. Although conscious and breathing normally, the patient was given gastric lavage, followed by activated carbon and atropine. He developed an episode of general seizures 6 hours after admission to the hospital. A second episode of seizures 28 hours later was fatal.

Between 1982 and 1999, 109 incidents of illness or injury with definite, probable or possible exposure to methidathion were reported to DPR's Pesticide Illness Surveillance Program (PISP) (Beauvais, 2004). No incidents were reported between 2000 and 2002. Thirty of these incidents were associated with exposure to methidathion alone while the rest were associated with exposure to methidathion in combination with other pesticides. Systemic effects were reported in 81 of the incidents (74% of the incidents) including nausea, vomiting, abdominal cramps, headache and dizziness. No deaths were associated with methidathion. The other incidents involved irritation or injuries to the eyes or skin. All but three incidents were occupational exposures, mostly involving handlers (36 applicators, 13 mixer/loader/applicators and 6 mixer/loaders). The rest of the occupational exposures were field workers which either entered a field treated with methidathion or experienced drift from an application of methidathion to a nearby field. Of the three non-occupational exposures, two were residents that lived near application sites and one was a cyclist that was accidently sprayed while riding past an orchard.

F. PHYSICAL AND CHEMICAL PROPERTIES

1.	Common Name:	Methidathion
2.	Chemical Name:	O,O-dimethyl-phosphorodithioate, S-ester with 4-(mercaptomethyl)-2-methoxy-Δ-1,3,4-thiadiazolin-5-one
3.	Trade Names:	Supracide®, Suprathion®, Medacide®, Ultracide®
4.	CAS Registry No.:	950-37-8
5.	Structural Formula:	
6.	Empirical Formula:	$C_6H_{11}N_2O_4PS_3$
7.	Molecular weight:	302.3 g
8.	Density:	1.445 g/ml (Newell, 1987)
9.	Solubility:	Water (22ºC) (Wyler, 1987): 220 mg/L Solvents (20ºC) (Lail, 1991): Cyclohexane: 850 g/L Acetone: 690 g/L Xylene: 600 g/L Ethanol: 260 g/L n-Octanol 53 g/L
10.	Vapor pressure:	3.37×10^{-6} mmHg at 25ºC (Rordorf, 1988)
11.	Octanol/water partition coefficient:	166 (log P_{ow} = 2.2) (Daly, 1987)
12.	Henry's law constant:	1.95×10^{-9} atm•m^3/mole at 22ºC (Leffingwell, 1989)

G. ENVIRONMENTAL FATE

<u>Hydrolysis</u>

The hydrolysis of methidathion was relatively stable at and below pH 7, but increased significantly above pH 7 (Burkhard, 1978). The half-lives at pH 1, 5, 7, 9 and 10 were 990, 880, 980, 295 and 45 hours, respectively, at 20ºC. The ultimate hydrolysis product was 2-methoxy-

1,3,4-thiadiazole-5(4H)-one or thiadiazole ring moiety (identified as the RH compound in Figure 1 in the Pharmacokinetics section).

Photolysis

The aqueous photodegradation of methidathion (10 ppm) over a 72 hour exposure period was examined using a mercury arc lamp (Suter, 1983). The estimated half-lives for the dark and light reactions were 157 and 103 hours, respectively. In another study, the photodegradation of methidathion (9.44 µg/ml) over a 15-day exposure period was examined in an aqueous buffered solution (pH 7) at 25ºC using a xenon lamp (Saxena, 1989a). The half-lives were 11.6, 8.2 and 45.9 days for the lamp (24 hrs/day), natural sunlight (12 hours/day), and dark (24 hrs/day) samples, respectively. The only degradation product identified in both of these studies was the thiadiazole ring.

Vapor phase photodegradation of ^{14}C-methidathion was examined using reaction chambers exposed to natural sunlight for up to 30 days (Kieatiwong, 1992). Petri dishes streaked with 100 µl samples of methidathion dissolved in acetonitrile (4.6 mg/ml) were placed in the reaction chambers. A maximum of 13.4% of applied dose was vaporized in samples exposed to sunlight after 30 days compared to only 6.2% in the dark control samples after 30 days. Ninety percent of the volatilized radioactivity collected from the walls of the chambers was the parent compound. In the dark control samples, 98% of the radioactivity from the chamber walls was the parent compound. The estimated half-life of methidathion in the vapor phase was 1.5 years for samples exposed to sunlight.

The photodegradation of methidathion (8.2 µg/g soil) on sandy loam soil from Tulare, California, was examined using continuous exposure (24 hrs/day) to artificial sunlight from a xenon lamp for a total of 17 days at 22.8ºC (Saxena, 1989b). The degradation appeared to be biphasic, with an initial rapid phase followed by a slower phase. The estimated half-life for the initial phase was 10.3 lamp days (equivalent to 8.96 natural sunlight days) and for the second phase was 24.7 lamp days (21.5 natural sunlight days). Two metabolites were isolated from the irradiated samples: the thiadiazole ring and the sulfoxide. A third unknown product and the parent compound were also isolated. In another soil photodegradation study, methidathion (10.3 µg/g) was applied to sandy loam soil samples from California and then exposed to artificial sunlight (xenon lamp) intermittently (12 hr light and dark cycles) at 25ºC for 30 days (Das, 1990). The half-life was estimated to be 40.6 days. The major metabolite was the thiadiazole ring. Three minor metabolites were identified including the oxygen analog, the sulfoxide and an unidentified third metabolite.

Soil Metabolism

The metabolism of ^{14}C-methidathion (9.44 ppm) was examined using sandy loam soil from Tulare, California, under aerobic and sequential aerobic/anaerobic conditions at 25ºC for 263 days (Saxena, 1990). On day 3, several aerobic samples were made anaerobic by flooding the soil with deoxygenated water. These samples were then placed in an incubation chamber and flushed with nitrogen. The estimated half-life was 3.1 days under aerobic conditions. The radioactive products were CO_2, 5 extractable compounds, and soil-bound residues. Of the 5 extractable compounds, two were identified as the thiadiazole ring and the sulfone. A third polar compound was later identified as a cyclic structure arising from the reaction of carbazic acid and cysteine. Two other polar compounds were considered transient metabolites and represented less than 5% of applied radioactivity on Day 11. It was not possible to calculate a half-life with anaerobic samples because radioactive products were only examined at two days (Days 30 and 62), but the ^{14}C-methidathion decreased from 41.4% on Day 0 (anaerobic conditions) to 2.0% on Day 30 and 0.6% on Day 62. The radioactive products identified from the anaerobic samples were similar to those identified from the aerobic samples, except the generation of CO_2 was slower.

Field Dissipation

The dissipation of a methidathion formulation, Supracide® 2E (no longer registered in California), was examined after application to an alfalfa field in Fresno County, California (Honeycutt, 1986a). The formulation was applied in a series of 12 applications at 1 lb a.i./acre per application, the last application was made in October. No rain fell during the period of application and the air temperatures ranged from 49 to 69°F. Methidathion was detected in the 0-6" soil layer with an average maximum concentration of 0.14 ppm. No residues were detected in the 0-6" layer by day 21. The estimated half-life was 8 days. Methidathion was also detected in the 6-12" soil layer on the day of the last application, but not on any subsequent days. Soil samples were also examined for the oxygen analog, but it was not found in either the 0-6" or 6-12" soil layer. The investigator suggested that because methidathion was only detected in the lower soil depth on the day of the last application, the dissipation of methidathion from the soil was not due to downward migration. The same investigator conducted another field dissipation study in which Supracide® 2E (4 lbs a.i./acre) was applied once to bareground (Immokalee fine sand soil) in Vero Beach, Florida, in May (91°F) (Honeycutt, 1986b). No rain fell on the day of application. Methidathion residues were detected in both the 0-6" and 6-12" soil layers collected on days 0-7. After day 7, the methidathion residues in both layers decreased until they were below the detection limit on day 21. The maximum concentration in the 0-6" layer was 1.8 ppm (day 3). The soil samples were not examined for any metabolites of methidathion. The estimated half-lives for methidathion were 5 and 8 days for the 0-6" and 6-12" soil layers, respectively.

The dissipation of methidathion was also examined after two applications of Supracide® 2E (5.5 lb a.i./acre/application) to citrus grown in sandy loam soil near Poplar, California, in July and August (Silvoy, 1991a). Methidathion was detected up to a depth of 18" on 0-3 days after application. Methidathion was detected in the 0-6" soil layer up to 60 days after application. The maximum concentration was 1.81 ppm on day 0 of the first application. The estimated half-life of methidathion was 9.23 days. The soil samples were also analyzed for the oxygen analog and thiadiazole ring. These metabolites were detected up to a depth of 24" and 18", respectively. This same investigator examined the dissipation of methidathion after a single application of Supracide® 2E (10 lb a.i./acre) to bareground (sandy loam soil) near Poplar, California, in July (Silvoy, 1991). Methidathion was detected up to a depth of 18" on days 0-14. Methidathion was detected in the 0-6" soil layer up to 30 days after application. The maximum concentration was 2.47 ppm on day 1. The estimated half-life for methidathion was 4.82 days. Soil samples were also analyzed for the oxygen analog and the thiadiazole ring. The oxygen analog was not detected in any soil samples at any time. The thiadiazole ring was only found in the 0-6" soil layer.

Soil Adsorption

The adsorption and desorption of methidathion was examined in batch equilibrium tests with four soil types (Mississippi loam, Maryland clay, Maryland sand, California sandy loam) (Martinson, 1988). The soil adsorption coefficients (K_d) were 0.154, 2.910, 6.527 and 8.680 for sand, loam, sandy loam and clay, respectively. The soil adsorption coefficients based on organic content (K_{oc}) were 29, 308, 410, and 859 for sand, clay, loam and sandy loam, respectively. The soil desorption coefficients (K_d) were 1.941, 4.104 and 8.864 for loam, sandy loam and clay, respectively. A desorption coefficient could not be calculated for methidathion in the sand soil because of negligible adsorption. The desorption coefficients based on organic content (K_{oc}) were 273, 314 and 540 for loam, clay, and sandy loam, respectively. These findings indicate that while methidathion readily adsorbs to the clay and sandy loam soils, the subsequent desorption is greater for the sandy loam (~50% of adsorbed material) compared to the clay (~20% of adsorbed material). Methidathion adsorbed moderately to the loam soil, but readily desorbed (~70% of adsorbed material).

Mobility

The soil leaching potential of methidathion was examined by column leaching with four different soil types (sand, sandy loam, loam and silty clay loam) (Shepler, 1992). ^{14}C-Methidathion was initially aged in sandy loam soil under aerobic conditions (25°C) for one half-life (4 days) before placing on top of the soil columns. At the end of the aging process, the soil samples contained approximately 57% methidathion, 0.5% sulfone, 4 unidentified metabolites and 27.4% bound residues. Ten percent, 14.4%, 16.3%, and 7.7% of the radioactivity was found in the leachate after addition to the sand, sandy loam, loam and silty clay loam soil columns, respectively. The rest remained on the column primarily in the first 6 cm of the soil column (77-93%). The K_d values were estimated to be 9.473, 5.658, 4.323, and 4.114 for the silty clay loam, sand, sandy loam, and loam soil, respectively.

The volatility of methidathion was determined by applying Supracide® 2E containing ^{14}C-methidathion (9.44 ppm) to moist, non-sterile loamy sand soil in Erlenmeyer flasks and incubating it at 25°C and 90% relative humidity for 30 days (Kesterson, 1991). The air was evacuated through two foam plugs and three gas dispersion traps which were sampled on days 3, 7, 10, 13, 17, 20, 23, 27, and 30. No methidathion was detected in the plugs or traps after day 3. The volatility rates ranged from 6.3×10^{-4} to 3.4×10^{-4} µg/cm^2/hr. The total radioactivity volatilized during the study period was 12.2% of the applied dose. Fifteen degradates were extracted from the foam plugs, but none were more than 2.9% of the applied dose. After 30 days, the soil was extracted for residues. Methidathion accounted for 2.5% of the applied dose while 3 other products which could not be definitively identified accounted for 24.1% of the applied dose. The investigators suggested that the volatility of methidathion in the environment is likely to be of little significance based on the lack of detectable residues in the plugs and traps after day 3.

Plant Metabolism

The metabolism of methidathion has been evaluated in several plants including cotton, artichokes, various rotational crops, and citrus trees (Simoneaux, 1991 & 1993). The major plant metabolites identified in cotton and artichokes included the oxygen analog, the desmonomethyl derivative, the thiadiazole ring, and various conjugates of the thiadiazole ring (cysteine, alanine, lactic acid, keto acid, acetic acid, hydroxyacetic acid). The major pathway in the metabolism of methidathion by plant involves the demethylation of one phosphate ester, followed by the cleavage of the methylene bridge to generate the thiadiazole ring and subsequent conjugation of the thiadiazole ring. The metabolism of methidathion appears to be the same in rotational crops and citrus trees, except pyruvic acid and glyoxylic acid were proposed as intermediates that degrade to lactic acid and hydroxyacetic acid, respectively, after residue analysis in citrus. No toxicity data was available for any of these plant metabolites, although the oxygen analog should be more toxic than the parent compound.

Groundwater Monitoring

Pursuant to the Pesticide Contamination Prevention Act (AB 2021), DPR has identified methidathion as a potential groundwater contaminant based on its high water solubility (> 3 ppm), low soil adsorption (K_{oc} < 1900 cm^3/g), and long hydrolysis half-life ($t_{1/2}$ > 14 days) (DPR, 1996b). However, methidathion has not been detected in any wells monitored by DPR from 1989 to 1996 (DPR, 1992, 1993a, 1994, 1995a, & 1997a).

Surface Water Monitoring

Methidathion residues were detected in 172 of 2,767 samples collected during surface water monitoring at 37 different locations in California between 1991 and 1998 (Ross, 1992, 1993; MacCoy *et al.*, 1995; Ross *et al.*, 1996; Bennet, 1997; Ganapathy *et al.*, 1997; Nordmark, 1997 &1998; Poletika and Robb, 1998; Ganapathy, 1999; Ross *et al.*, 1999; U.S. Geological Survey, in preparation). Most of the samples were collected along the Sacramento River (670 samples from 4 locations), the San Joaquin River (774 samples from 7 locations) and the Orestimba Creek which is a tributary of the San Joaquin River (1,006 samples from 3 locations). Assuming the samples with non-detectable residues were equal to the limit of quantitation (LOQ), the mean residue level was 0.042 ppb. The LOQ ranged from 0.0024 to 0.1 ppb. The maximum residue level detected was 12.39 ppb; however, the 95th percentile of the residue levels was only 0.654 ppb.

II. TOXICOLOGY PROFILE

A. PHARMACOKINETICS

Summary

Methidathion is readily absorbed, metabolized and excreted in rats after oral exposure. The major routes of excretion were urine and CO_2. Fecal excretion represented a minor route. Based on the amount excreted in the urine, CO_2 and feces, the oral absorption was assumed to be 100%. Methidathion was also readily absorbed by the dermal route. Based on deficiencies in the available dermal absorption study in mice, a default value of 50% was assumed for dermal absorption. Several urinary metabolites were identified in the rat, including the cysteine conjugate, and the sulfide, sulfoxide, sulfone, RH, and desmonomethyl derivatives.

Absorption

Oral: Groups of 5 rats/sex/dose were administered a single dose of ^{14}C-methidathion (labeled on the carbonyl carbon of the thiadiazole ring) by oral gavage at 0.314 or 2.985 mg/kg (Szolics, 1987). A third group was administered unlabeled methidathion by oral gavage at 0.25 mg/kg for 14 days and then given single dose of ^{14}C-methidathion by oral gavage at 0.309 mg/kg on day 15. Urine and feces was collected for 7 days following the final application. The CO_2 excretion was estimated in this study based on data from a preliminary study using 2 rats/sex/dose at 0.295 mg/kg and at 2.949 mg/kg. In the preliminary study, 75-89% of the administered dose was excreted in the first 24 hours whereas in the main study 63-73% of the administered dose was excreted in the first 24 hours. However, there was a significant difference in the recoveries between the main study (76-93%) and the preliminary study (99-102%). The author suggested that the low recoveries in the main study were due to losses during the storage of urine samples for three months prior to analysis. Since the CO_2 excretion was not actually monitored in the main study, it is uncertain if the recoveries were lower from the losses in the urinary samples or from the CO_2 excretion being higher than estimated. A comparison of these two studies is also difficult because different laboratories conducted these studies and different breeders provided the Sprague-Dawley rats used which could have slight genetic differences in their metabolism of methidathion. Despite having fewer animals per dose group, the data from the preliminary study was used to estimate the percent oral absorption since the recoveries were better and the CO_2 excretion was measured. The radioactivity in the feces was assumed to be due primarily to biliary excretion because of similar fecal excretion rates with dermal application (Simoneaux and Marco, 1984). The combined urinary, fecal and CO_2 excretion in the preliminary study ranged from 98 -102%. Therefore, the oral absorption rate was assumed to be 100%.

Dermal: ^{14}C-Methidathion (labeled on the carbonyl carbon of the thiadiazole ring) was applied to shaved backs of 4 mice/sex in either an acetone solution or formulated product containing petroleum hydrocarbon with an emulsifier at 12 mg/kg over an 0.25 sq. inch area (Simoneaux and Marco, 1984). Urine, feces, and CO_2 excretion were monitored for 72 hours after application. With this route of application, CO_2 was the main route of excretion ranging from 51-56% with the formulated product to 61-64% with the acetone solution. Urinary excretion was significantly lower ranging from 14-15% with the acetone solution to 16-23% with the formulated product. The combined urinary, fecal, and CO_2 excretion after 72 hours ranged from 75.4% for females treated with the formulated product to 82.1% for males treated with the acetone solution. It is interesting that while the amount absorbed is not that different between the two formulations, the pathways by which they are metabolized changed slightly. Due to the use of organic solvents and the testing of only one dose level, DPR found this study unacceptable for estimating dermal absorption (Beauvais, 2004). Therefore, DPR assumed a default value of 50% for dermal absorption.

Distribution

In the preliminary rat metabolism study conducted by Szolics (1987), the total amount excreted within the first 24 hours ranged from 75% in females at 2.949 mg/kg to 89% in males at 0.295 mg/kg. In the main metabolism study, the total amount excreted within the first 24 hours was estimated to be 63% in males at 0.295 mg/kg to 73% in females at 2.949 mg/kg assuming similar CO_2 excretion rates to the preliminary study. Elimination half-lives were not calculated for the preliminary metabolism study, but are obviously less than 24 hours. Using the CO_2 excretion data from the preliminary study, the estimated elimination half-lives for the main rat metabolism study ranged from 7.4 hours in females at 0.295 mg/kg to 9.7 hours in males receiving 0.295 mg/kg/day for 14 days. In the preliminary study, only carcass residue levels were measured 7 days after dosing, ranging from non-detectable in both sexes at 0.295 mg/kg to 0.93% of administered dose in females at 2.949 mg/kg. In the main study, tissue residue levels ranged from 0.53% of administered dose in the females at 2.949 mg/kg to 1.14% in males at 0.295 mg/kg 7 days after the last dose. The vast majority of the radioactivity (0.40-0.98% of administered dose) was found in the carcass. No other tissue levels exceeded 0.1% of the administered dose.

Biotransformation

Four male rats were administered 0.642 mg ^{14}C-labeled methidathion by oral gavage (Cassidy *et al.*, 1969). The ^{14}C-label was on the carbonyl carbon of the thiadiazole ring. Urine samples were collected during the first 24 hours after dosing and analyzed for metabolites. Six radioactive urinary metabolites were isolated, but only three were identified. The three identified urinary metabolites were the sulfoxide, the sulfone, and the desmethyl derivative which represented 52%, 13%, and 7% of the radioactivity in the urine, respectively.

The *in vitro* metabolism of ^{14}C-methidathion (labeled on the carbonyl carbon) was examined using rat and mouse liver subcellular fractions (Chopade and Dauterman, 1981). Methidathion underwent *O*-demethylation via the glutathione *S*-transferases forming des(mono)methyl methidathion. Methidathion also underwent oxidative desulfuration via the mixed function oxidase system to form the oxygen analog. Methoxythiadiazolin (RH compound) was also formed by the mixed function oxidase system, but the exact mechanism is unknown. The P-S bond of methidathion and its oxygen analog were hydrolyzed forming a reactive mercaptomethyl intermediate which underwent *S*-methylation to form the sulfide. The sulfide was then oxidized to the sulfoxide by the FAD-dependent monooxygenase system; however, the sulfoxide was oxidized to the sulfone by the mixed function oxidase system. There did not appear to be any significant species differences in metabolism between rats and mice.

Prior to the conduct of the main rat metabolism study, Szolics (1987) conducted three pilot studies in which methidathion was administered to rats with the ^{14}C-label on different carbons of the thiadiazole ring: the carbonyl carbon, the methoxy group carbon, and the carbon adjacent to the methoxy group. The amount excreted in the respiratory gases was lowest when the ^{14}C-label was adjacent to the methoxy carbon (10-12%). Significantly higher amounts of radioactivity were found in the respiratory gases when the ^{14}C-label was on the carbonyl carbon (33-44%) or the methoxy group carbon (40-44%). With the ^{14}C-label on the methoxy group carbon, an additional unknown ^{14}C-labeled material other than CO_2 was found in the trapping solution. The investigators suggested it might be another volatile gas such as methane. Analysis of the urinary metabolites indicated that approximately two-thirds were organic soluble and one third aqueous soluble, regardless of the position of the ^{14}C-label. The sulfide, sulfoxide, sulfone, and RH derivatives were the major urinary metabolites in the organic soluble fraction. The cysteine conjugate and the desmonomethyl derivative were the major urinary metabolites in the aqueous soluble fraction. With the ^{14}C-label on the carbonyl carbon and the carbon adjacent to the methoxy group, the major urinary metabolite was the sulfide. With the ^{14}C-label on the methoxy carbon, the sulfoxide was the major urinary metabolite. The parent compound was found only with the ^{14}C-label on the carbonyl carbon (0.7%). The oxygen analog was found when the ^{14}C-label was on either the methoxy carbon or adjacent to the methoxy carbon (0.2-0.8%).

Based on these findings, Szolics (1987) proposed a metabolic pathway for methidathion in the rat (Figure 1). The first step in the major metabolic pathway is the hydrolysis of the S-P bond to form the reactive mercaptomethyl intermediate which undergoes S-methylation to form the sulfide. The sulfide then undergoes oxidation to form the sulfoxide and sulfone. Szolics proposed a secondary metabolic pathway in which the mercaptomethyl intermediate undergoes conjugation with glutathione to form the glutathione conjugate and its derivatives such as the cysteine conjugate. Another proposed secondary metabolic pathway was the *O*-demethylation to form the desmonomethyl derivative. The oxidative desulfuration of methidathion to the oxygen analog was considered a minor metabolic pathway. Szolics suggested that the RH metabolite could be derived from a variety of intermediates. The metabolic pathway proposed by Szolics (1987) for methidathion is similar to one proposed by Chopade and Dauterman (1981), although Chopade and Dauterman considered the *O*-demethylation of methidathion to the desmonomethyl methidathion to be the major pathway.

<u>Excretion</u>

The two major routes of excretion appear to be the urine and CO_2 in both the main study and the preliminary study conducted by Szolics (1987). In the preliminary study, the mean urinary excretion was essentially identical at both 0.295 and 2.949 mg/kg, but varied slightly between sexes (M: 57%; F: 54%). In the main study, the mean urinary excretion was significantly lower, ranging from 30% in males at 0.295 mg/kg to 42% in males at 2.949 mg/kg, except in females at 2.949 mg/kg which excreted 57%. As mentioned previously under the discussion for oral absorption, Szolics suggested the lower recoveries in the main study were due to losses in the urine during a 3-month storage period. However, another possible explanation may be slight genetic differences in the metabolism of methidathion due to different sources of Sprague-Dawley rats used in the two studies. In the preliminary study, the mean CO_2 excretion was slightly higher at 0.295 mg/kg (M: 41%; F: 44%) than at 2.949 mg/kg (M: 34%; F:32%),

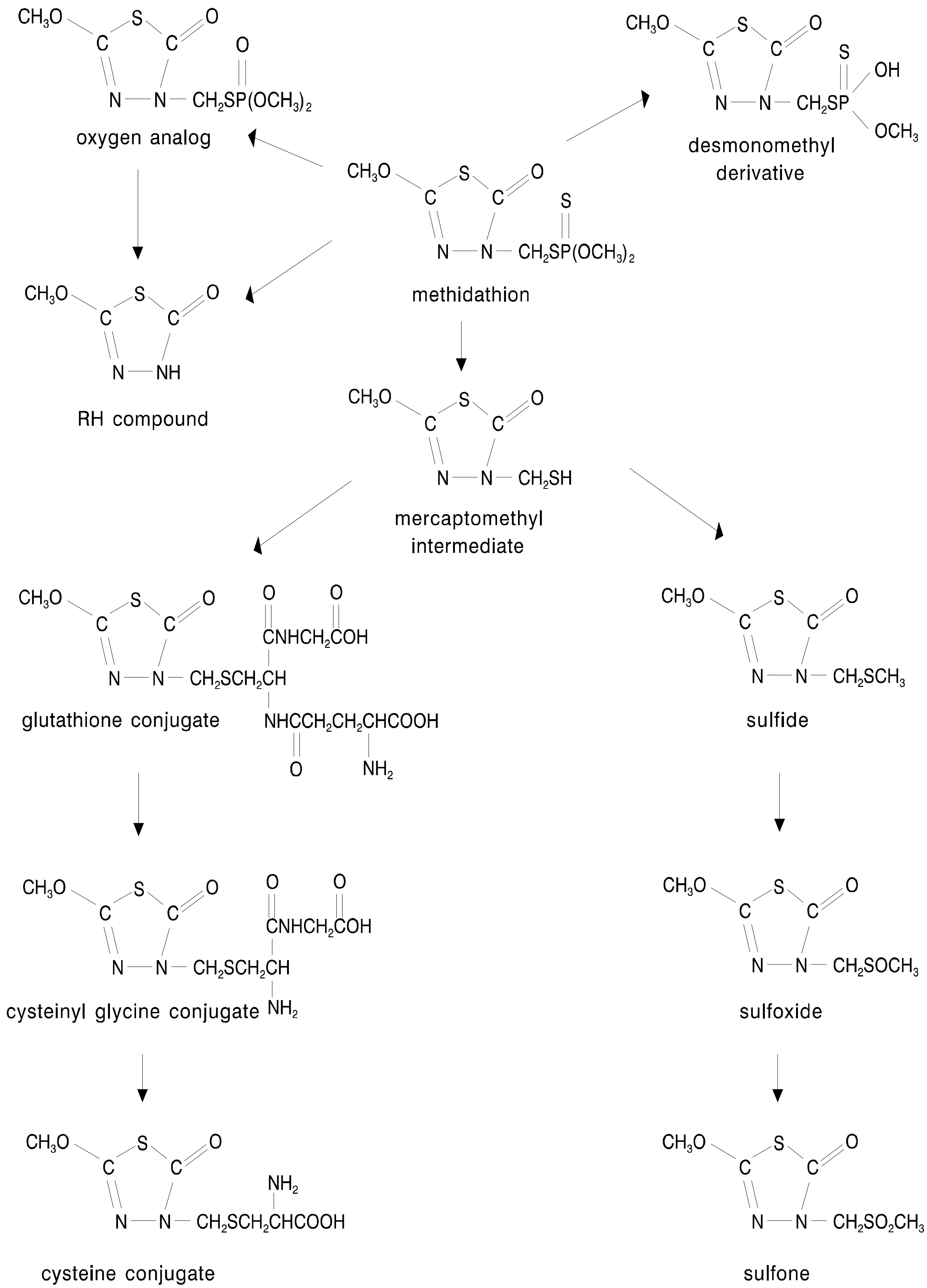


Figure 1. Proposed Metabolic Pathway for Methidathion in Rats (Szolics, 1987)

whereas the mean fecal excretion was lower at 0.295 mg/kg (M: 5%; F: 3%) than at 2.949 mg/kg (M: 8%; F: 12%). Since the CO_2 excretion was not measured in the main study, it is unknown if the CO_2 excretion in this study also varied with dose level or with repeated exposure. The mean fecal excretion in the main study was relatively similar between dosing regimens, but it tended to be slightly higher in the males (0.78-1.14%) than the females (0.53-0.72%).

B. ACUTE TOXICITY

Summary

Only studies on the acute oral and dermal toxicity of technical grade methidathion were available. The clinical signs observed with the technical material were typical cholinergic signs including tremors, ataxia, fasciculations, difficulty in breathing, salivation, lacrimation and exophthalmos. There were insufficient data for establishing a No-Observed-Effect Level (NOEL) or Lowest-Observed-Effect Level (LOEL) for the technical grade material. Based on the limited data for the technical grade material, it appears to be a Category I pesticide. More complete data were available for the formulations. The wettable powder formulation was a Category II pesticide based on its oral toxicity and inhalation toxicity. The emulsifiable concentrates were considered a Category I pesticide based on its oral toxicity and severe eye irritation. There is some evidence which suggests an increased sensitivity to methidathion in young animals. A synergistic increase in the toxicity of methidathion was observed with 6 other organophosphate chemicals.

Technical Grade Methidathion

Table 1 summarizes the acute toxicity studies for technical grade methidathion. The data available on the technical material are limited to a brief summary of the acute oral and dermal toxicity. The purity of the technical grade material was not reported. The effects reported included dizziness, ataxia, irregular and increased respiration, dyspnea, fasciculations, trembling, salivation, exophthalmos, and death. Based on a study conducted by Gaines and Linder (1986), weanling rats appear to be more sensitive to the lethality of methidathion than adults. A study was conducted in pigeons which compared the acute oral and dermal toxicity of several organophosphates used as dormant sprays in orchards, including ethyl parathion, diazinon and methidathion (Henderson *et al.*, 1994). Methidathion was the least toxic of these three organophosphates based on its lethal oral dose range (30-40 mg/kg). The investigators also applied these three organophosphate pesticides to the feet of pigeons to simulate exposure in hawks from perching in orchards. With the dermal exposure, only birds given ethyl parathion at ≥ 59 mg/kg died. They found no significant plasma ChE inhibition at the highest dose tested of methidathion, 37 mg/kg, despite mild signs (not specified) of organophosphate poisoning. In another study, a significant reduction in plasma ChE activity (71% of controls) was seen in pigeons administered a single oral dose of methidathion at 10 mg/kg (Bartkowiak and Wilson, 1995). Plasma carboxylesterase activity was not affected at this dose level. No other dose levels were tested nor were any other endpoints evaluated in this study. Insufficient information was provided in all of these acute toxicity studies for methidathion to establish a LOEL or NOEL for an acute, single dose exposure scenario. No data were available on the ocular or dermal irritation potential of the technical grade methidathion. One dermal sensitization study was

Table 1. The Acute Toxicity of Technical Grade Methidathion

Species	Sex	Results	References[a]
		Acute Oral LD_{50}	
Rat	NR	25-48 mg/kg	1
Mouse	NR	26-32 mg/kg	
Rabbit	NR	63-80 mg/kg	
Guinea Pig	NR	25 mg/kg	
Hamster	NR	30 mg/kg	
Rat, weanling	M	21 mg/kg	2
adult	M	31 mg/kg	
	F	32 mg/kg	
Pigeon	NR	30-40 mg/kg	3
		Acute Dermal LD_{50}	
Rabbit	M/F	140-155 mg/kg	1
Rat	M	94 mg/kg	2
	F	85 mg/kg	
		Dermal Sensitization	
Guinea Pig	F	Moderate-Severe	4

a References: 1. Geigy, 1964; 2. Gaines and Linder, 1986; 3. Henderson *et al.*, 1994; 4. Matsushita and Aoyama, 1981.

available that suggests that methidathion is a potential sensitizer (Matsushita *et al.*, 1985). These investigators also examined if exposure to methidathion during the induction phase causes a cross reaction when later challenged with benomyl, DDVP, and naled. There was some evidence of a cross reaction with DDVP and naled, but no cross reaction with benomyl.

The effect of methidathion on Na^+/K^+-ATPase, Ca^{2+}/Mg^{2+}-ATPase, cholesterol and phospholipid levels in RBC membranes was evaluated in rats administered 1, 3, 5 or 7 daily doses at 2 mg/kg (El-Dawy *et al.*, 1995). There was a significant reduction in the activity of both ATPases with 1 to 7 doses. The investigators suggested that this reduction in ATPase activity could result in the preservation of cell energy and ions. The cholesterol levels in the membranes was also elevated with one or more doses of methidathion. By contrast, the phospholipid levels decreased with 3 or more doses. The investigators suggested that these changes in cholesteroland phospholipid levels may be an adaptive response to increase the resistance of the RBCs to osmotic lysis.

<u>Methidathion Formulations</u>

The acute toxicity of the Supracide® wettable powder is summarized in Table 2. The primary clinical signs observed with inhalation exposure included hypoactivity, piloerection,

Table 2. The Acute Toxicity of Methidathion (25%) Wettable Powder

Species	Sex	Results	References[a]
Acute Inhalation LC_{50}			
Rat	M	0.57 mg/L (4-hr, whole body)	1*
	F	0.11 mg/L (4-hr, whole body)	
Acute Oral LD_{50}			
Rat	M	94 mg/kg	2*
	F	53 mg/kg	
Acute Dermal LD_{50}			
Rabbit	M/F	> 2,020 mg/kg	3*
Primary Dermal Irritation			
Rabbit	M/F	Non-Irritant	4*
Primary Eye Irritation			
Rabbit	M/F	Moderate Irritant	5*
Dermal Sensitization			
Guinea Pig	M	Non-Sensitizer	6

a References: 1. Holbert, 1992; 2. Kuhn, 1992a; 3. Kuhn, 1992b; 4. Kuhn, 1992c; 5. Kuhn, 1992d; 6. Kuhn, 1992e.
* Acceptable study based on the FIFRA guidelines.

tremors, salivation, unsteady gait, exophthalmos, polyuria, nasal discharge, and lacrimation (Holbert, 1992). Gross necropsy findings included discoloration of the contents of the gastrointestinal tract, discoloration of the liver and lungs, lungs swollen, and small intestine distended with gas. Similar clinical and gross pathological observations were observed with oral exposure to the Supracide® wettable powder, except they were less pronounced (Kuhn, 1992a). With dermal exposure to the Supracide® wettable powder, the only effect observed was decreased defecation in one of five males (Kuhn, 1992b). No erythema or edema was observed with dermal exposure to the Supracide® wettable powder (Kuhn, 1992c). Slight corneal opacity was observed in one of six rabbits exposed to the Supracide® wettable powder (Kuhn, 1992d). No other ocular effects were seen. No sensitization response was observed in guinea pigs after exposure to the Supracide® wettable powder (Kuhn, 1992e).

Several acute studies were conducted in turkeys in which young (6-8 weeks) and adult (16-18 weeks) turkeys were administered the 25% wettable powder by the oral or dermal route (Schlinke and Palmer, 1971; Radeleff and Kunz, 1972). In the study conducted by Schlinke and Palmer (1971), 6-week-old turkeys appeared to be more sensitive to methidathion based on a lower acute oral NOEL (10 mg a.i./kg) for unspecified signs compared to 16-week-old turkeys (20 mg a.i./kg). However, in another study conducted by Radeleff and Kunz (1972), 18-week-old turkeys appeared more sensitive with an acute oral NOEL of 10 mg a.i./kg for unspecified signs compared to 15 mg a.i./kg in 8-week-old turkeys. A similar comparison of dermal NOELs was not possible in either of these studies because of the limited number of dose levels tested with dermal exposure.

The acute toxicity of Supracide® emulsifiable concentrate was similar to the wettable powder with the exception of the ocular and dermal irritation (Table 3). The clinical signs observed with inhalation, oral and dermal exposure to the emulsifiable concentrate were similar to those observed with the wettable powder with similar LC_{50}/LD_{50} values (Holbert, 1989; Kuhn, 1989a&b). Unlike the wettable powder, the Supracide® emulsifiable concentrate caused moderate dermal irritation including well-defined erythema lasting up to 21 days and slight edema lasting up to 14 days (Kuhn, 1989c). The Supracide® emulsifiable concentration also caused severe eye irritation including complete corneal opacity in some rabbits lasting up to 21 days, iritis that lasted up to 17 days and conjunctivitis that lasted up to 21 days (Kuhn, 1989d). Like the wettable powder, there was no evidence of dermal sensitization in guinea pigs with the Supracide® emulsifiable concentrate (Kuhn, 1989e).

Table 3. The Acute Toxicity of Methidathion (22.5%) Emulsifiable Concentrate

Species	Sex	Results	References[a]
		Acute Inhalation LC_{50}	
Rat	M	0.575 mg/L (4-hr, whole body)	1*
	F	0.167 mg/L (4-hr, whole body)	
		Acute Oral LD_{50}	
Rat	M	111 mg/kg	2*
	F	22 mg/kg	
		Acute Dermal LD_{50}	
Rabbit	M	> 1,990 mg/kg	3*
	F	2,240 mg/kg	
		Primary Dermal Irritation	
Rabbit	M/F	Moderate Irritant	4*
		Primary Eye Irritation	
Rabbit	M/F	Severe Irritant	5*
		Dermal Sensitization	
Guinea Pig	M	Non-Sensitizer	6*

a References: 1. Holbert, 1989; 2. Kuhn, 1989a; 3. Kuhn, 1989b; 4. Kuhn, 1989c; 5. Kuhn, 1989d; 6. Kuhn, 1989e.
* Acceptable study based on the FIFRA guidelines.

Synergism

Synergism is sometimes observed when two organophosphate chemicals are given simultaneously. The toxicity of a 25% methidathion wettable powder formulation was evaluated in rats when co-administered with one of 17 compounds (carbophenothion, demeton, coumaphos, diazinon, azinphos-methyl, dioxathion, EPN, ethion, malathion, mevinphos, methyl parathion, carbaryl, ethyl parathion, fenchlorphos, schradan, disulfoton and S,S,S-tributyl phosphorotrithioite) at 1/8, 1/4 and 1/2 of their LD_{50} dose (Woodard Research, 1966a). A synergistic increase in the toxicity of methidathion was reported with 6 compounds (carbaryl, mevinphos, azinphos-methyl, methyl parathion, fenchlorphos and disulfoton). No details were provided on how the toxicity of methidathion was evaluated.

C. SUBCHRONIC TOXICITY

Summary

Twelve subchronic toxicity studies were available for methidathion, 6 oral studies in rats, mice and turkeys and 6 dermal studies in rats, rabbits and turkeys. Clinical signs included lethargy, anorexia, labored or rapid breathing, hunched posture, ataxia, tremors, soft feces, and low body temperature. Reductions in body weights and food consumption were also seen. Pathological findings included changes in hematological values suggesting anemia, changes in serum enzymes suggesting liver toxicity, reduced brain cholinesterase (ChE) activity, and lesions in the liver, gallbladder, stomach and heart. ChE inhibition was one of the most sensitive endpoints, when measured, with subchronic exposure. The lowest NOEL was 0.2 mg/kg/day based on a reduction in ChE activity in rats in several studies of varying length from the same laboratory. None of the subchronic studies met FIFRA guidelines.

Gavage-Rat

Ten rats/dose (sex and strain not reported) were administered methidathion (purity not reported) at 0.25, 0.83, 2.5, 8.3, 16.6 or 33.2 mg/kg/day by oral gavage in propylene glycol daily for 4 weeks (Geigy, 1964). Five and 10 rats died within the first 4 days of exposure at 16.6 and 33.2 mg/kg/day, respectively. Consequently, all survivors at these dose levels were sacrificed at 2 weeks. No changes in body weights were observed at or below 8.3 mg/kg/day. Rats at 8.3 mg/kg/day and higher were reported to have clinical signs of toxicity, but no details were provided. Plasma ChE activity was only reduced at 8.3 mg/kg/day (76% and 73% of reported normal values at 2 and 4 weeks, respectively). RBC ChE activity was reduced at 0.83, 2.5 and 8.3 mg/kg/day (62%, 51% and 6% of reported normal values at 2 weeks, respectively; 77%, 46% and 16% of reported normal values at 4 weeks, respectively). Based on the limited information provided, the NOEL for this study appears to be 0.25 mg/kg/day based on the reduced RBC ChE activity (62% and 77% of reported normal values at 2 and 4 weeks, respectively) at 0.83 mg/kg/day. This study had major deficiencies based on the FIFRA guidelines for subchronic studies; however, it was conducted before the guidelines existed. The deficiencies included no analysis of test article or dosing material, no control animals, inadequate number of animals per dose level, inadequate exposure duration, limited clinical chemistry analyses, no hematology or urinalysis, no pathological examination, no summary of body weights and clinical signs by treatment group, and no individual data.

Gavage-Rat

Groups of 5 rats (strain not specified)/sex/dose were administered technical grade methidathion (purity not reported) at 2.5, 5, 10 or 20 mg/kg/day by oral gavage in gum arabic on 6 days/week for 4 weeks (Geigy, 1964). Thirteen animals died (sex not indicated) during the study, 4 at 10 mg/kg/day and 9 at 20 mg/kg/day. Animals at 5 mg/kg/day exhibited signs which were described as typical of cholinesterase inhibition (no other details provided). Body weight reductions were seen although the severity was difficult to estimate from the figures provided. At 5 mg/kg/day and higher, centro-medio-lobular fatty deposits in liver cells were seen microscopically. Based on the limited information provided, the tentative NOEL for this study appears to be 2.5 mg/kg/day. This study had numerous major deficiencies including no analysis of test article or dosing material, no control animals, inadequate number of animals per dose level, inadequate exposure duration, no clinical pathology analyses, no summary of body weights, clinical signs, and pathological findings by treatment group, and no individual data.

Gavage-Turkey

The oral toxicity of a 25% methidathion wettable powder was evaluated in 5 6-week-old turkeys (sex not reported)/dose at 0, 2.5, 5, 10 and 20 mg a.i./kg/day for 10 days (Schlinke and Palmer, 1971). One bird died at 20 mg/kg/day. No other effects were reported. The NOEL in the 6-week-old turkeys appears to be 10 mg/kg/day. The 25% wettable powder was also administered to 5 16-week-old turkeys/dose at 0, 5, 10 and 20 mg a.i./kg/day for 10 days. Three deaths and unspecified signs in the other two birds were seen at 20 mg/kg/day. Signs of toxicity were also seen in one bird at 10 mg/kg. The NOEL in 16-week-old turkeys appears to be 5 mg/kg/day. These data suggest that the adults are more sensitive to methidathion with repeated exposure. This is in contrast with their findings in turkeys after acute exposure and with another study in rats after acute exposure (Gaines and Linder, 1986). In all cases, the differences in NOELs or LD_{50} values were small and may be the result of random chance given the small number of animals tested rather than any real difference in sensitivity. This study had major deficiencies based on the FIFRA guidelines for subchronic studies including no analysis of test article and dosing material, inadequate exposure period, inadequate number of animals, inadequate summary of clinical signs, no pathological examination, and no individual data.

Diet-Rat

Methidathion (purity not reported) was administered to 24 rats (strain not reported)/sex/dose in the diet at 0, 1, 4, 16 or 64 ppm (0, 0.05, 0.2, 0.8 or 3.2 mg/kg/day, respectively[1]) for 4 to 22 weeks (Geigy, 1964). Animals in each group (numbers not reported) were sacrificed at different times (not specified) during the study for cholinesterase analyses. In addition, unspecified blood and urine analyses were performed on rats at 64 ppm during the 14th week. There was one death in each of the treatment groups at 4 ppm and higher. There were no

[1] Estimated assuming for a rat that 1 ppm in the diet is equivalent to 0.05 mg/kg/day (FDA, 1959).

reported effects on food intake, body weight, hematology, urine analysis, and pathological findings. There was no indication if there were any clinical signs. It was reported that there was no effect on ChE activity at 4 ppm, a moderate reduction (25-30%) at 16 ppm and strong reduction (70-80%) at 64 ppm. However, no details were provided about which ChE was reduced except that plasma ChE activity was reduced to a lesser extent than RBC or brain ChE activity. Based on the limited information provided, the NOEL was tentatively identified as 4 ppm (0.2 mg/kg/day) based on possible plasma, RBC and brain ChE inhibition at 16 ppm. The study had numerous major deficiencies including no analysis of test article or dosing material, no clinical chemistry analyses, no summary of body weights, clinical signs, urinalysis, hematology, cholinesterase activity and pathological findings by treatment group, and no individual data.

Diet-Rat

Twenty rats (strain not reported)/sex/dose were administered methidathion (purity not reported) dissolved in propylene glycol and mixed in the diet at 0 (two control groups with and without propylene glycol), 0.5, 2, 10, 50 or 250 ppm (0.05-0.06, 0.2-0.24, 1.1-1.2, 5.5-6.0 or 30 mg/kg/day, respectively) for 6 months (Geigy, 1964). Several males died during the study including 2 controls, 1 at 2 ppm, 2 at 20 ppm and 2 at 250 ppm. These deaths were all attributed to a severe chronic respiratory disease and was not considered treatment-related. The only clinical signs reported was fine fibrillation in the extremities and hyperexcitability at 250 ppm. A slight transient reduction in body weights (percentage or mean body weights not reported) was reported at 250 ppm. RBC ChE activity was reduced (percentage not reported) at 10 ppm and higher. Plasma, brain, muscles, liver and kidney ChE were reduced only at 250 ppm. No abnormal pathological lesions were reported, although the histopathological results were not available at the time of the report. Based on the limited data provided, the NOEL appears to be 2 ppm (0.2 mg/kg/day) based on the reduced RBC ChE activity (percentage not reported). The study had numerous major deficiencies including no analysis of test article or dosing material, limited clinical chemistry analyses, no hematology or urinalysis, no histopathology, no summary of body weights, clinical signs, cholinesterase activity, and pathological findings by treatment group, and no individual data.

Diet-Mice

Technical grade methidathion (93.8% purity) was administered to 5 Charles River strain albino mice/sex/dose in the diet at 0, 0.3, 1, 3, 10, 30, 100, 300, 1,000 or 3,000 ppm (M: 0, 0.059, 0.23, 0.60, 2.3, 6.5, 20, 62, 219 or 276 mg/kg/day; F: 0, 0.045, 0.17, 0.54, 1.8, 4.2, 18, 42, 330 or 574 mg/kg/day, respectively) for 28 days (Albanese, 1976). Five mice (2 males, 3 females) at 1,000 ppm and all the mice at 3,000 ppm died during the first few weeks of the study. Generalized weakness was observed in mice at 1,000 ppm and higher. No other clinical signs were reported. Surviving mice at 1,000 ppm had reduced mean body weights (M: 29%; F: 16%) after 28 days. Plasma ChE activity was only reduced at 300 ppm (M: 73%; F: 79% of controls). RBC ChE activity was reduced at 100 ppm (F: 57% of controls) and 300 ppm (M: 87%; F: 66% of controls). Brain ChE activity was also reduced at 100 ppm (M: 49%; F: 65% of controls) and 300 ppm (M: 29%; F: 34% of controls). No gross pathological lesions were seen. With the limited data provided, the tentative NOEL appears to be 30 ppm (4.2 mg/kg/day) based on reduced RBC ChE activity (F: 57% of controls) and brain ChE activity (M: 49%; F: 65% of controls) at 100 ppm. This study had major deficiencies including no analysis of dosing material, inadequate number of animals per treatment group, inadequate clinical chemistry, no hematology, urinalysis or histopathology, and no individual data.

Dermal-Rat

Methidathion technical material (purity not reported), 40% wettable powder and 40% emulsifiable concentrate were each applied in gum arabic to 20 cm^2 shaved dorsal skin of 3 rats (strain not reported)/sex/formulation at 1.50 mg/kg/day (technical material) or 54 mg/kg/day (formulations) for 5 successive days (Geigy, 1964). It does not appear any protective covering was used since the rats were restrained for 3 hours during exposure and then the skin was wiped with a damp sponge. Typical acute clinical signs (not described) were seen, but no mortalities or dermal irritation were reported. A NOEL could not be established for this study based on the limited information provided. The study had numerous major deficiencies including no analysis of test article or dosing material, inadequate number of animals, inadequate number of treatment groups, no controls, inadequate exposure duration, no body weight data, no pathology, no summary of clinical signs by treatment group, and no individual data.

Dermal-Rat

Technical grade methidathion (purity not reported) in gum arabic was applied to the shaved skin of 5 rats(strain not specified)/sex/dose at 1.5, 3, 6 or 12 mg/kg/day on 5 days/week for 4 weeks (Geigy, 1964). It does not appear any protective covering was used since the rats were immobilized for 3 hours during exposure after which the skin was wiped with a damp sponge. No deaths, clinical signs or dermal irritation was seen. Body weights were also normal. Based on this limited information, the tentative NOEL appears to be 12 mg/kg/day. The study had numerous major deficiencies including no analysis of test article or dosing material, inadequate number of animals, no controls, no pathology, no summary of body weights and clinical signs by treatment group, and no individual data.

Dermal-Rabbit

Methidathion (purity not reported) was applied topically (non-occlusive exposure) to the clipped back and flanks of 5 New Zealand white rabbits/sex/dose at 0, 1, 5, or 20 mg/kg/day for 6 hr/day for 22 consecutive days (Folinusz *et al.*, 1986). A control male and a female at 5 mg/kg/day were injured during the study and were either sacrificed in moribund condition or died. Neither of these deaths were considered treatment-related. Diarrhea or soft feces was observed on more than one day in several treated animals (1 male at 1 mg/kg/day, 2 males at 5 mg/kg/day, 1 male and 1 female at 20 mg/kg/day). It is unclear if the diarrhea was treatment-related, although it is possible. A male at 20 mg/kg/day also had reduced activity on days 6-19. A papular rash was observed in several animals (1 male and 2 females at 1 mg/kg/day, 1 male at 5 mg/kg/day, 1 male and 1 female at 20 mg/kg/day) from days 16 to 24. Slight reductions in mean body weights (5%) were observed at 20 mg/kg/day, but were not statistically significant. No other treatment-related effect on food consumption, clinical chemistry, hematology or pathology were noted. The NOEL appears to be 20 mg/kg/day since the effects seen at this dose level were minor and not clearly treatment related. The study had a few deficiencies in that the purity of the methidathion was not reported and a maximum tolerated dose (MTD) was not clearly established.

Dermal-Rabbit

A range-finding study was conducted in which methidathion (95% purity) was applied to the clipped backs of 2 New Zealand White rabbits/sex/dose for 6 hours/day for 10 days at 0 (vehicle polyethylene glycol 400), 125, 250, 350, 500 or 740 mg/kg/day (Osherhoff, 1987a). The application site was covered with an occlusive binder during the 6-hr exposure period and then wiped clean after the binder was removed. The mortality rate was 25%, 50%, 50%, 75%, 100% and 100% of animals at 0, 125, 350, 250, 500, and 750 mg/kg/day, respectively. The onset of deaths was usually earlier at the higher dose levels. Clinical signs included anorexia, depression, labored or rapid breathing, hunched posture, ataxia, tremors, and prostration. A reduction in body weight, body weight gains, and food consumption were seen in the treatment groups relative to controls. Plasma, RBC and brain ChE activity were significantly reduced in survivors at 125 mg/kg/day (M: 16-22%; F: 15-17% of controls), 250 mg/kg/day (M: 9-17%; F: 7-16% of controls) and 350 mg/kg/day (F: 9-14% of controls) after 10 days. Interpretation of these reductions was difficult because of the small number of animals per group and the high mortality rate. No treatment-related changes in organ weights or gross pathological lesions were seen. A NOEL was not established in this study based on the mortalities at the lowest dose, 125 mg/kg/day. This study had several major deficiencies including inadequate number of animals per group, inadequate exposure duration, inadequate clinical chemistry, no hematology, and no histopathology.

Dermal-Rabbit

Five New Zealand White rabbits/sex/dose were administered methidathion (95% purity) dermally (rubber dam occlusion) to their clipped backs at 0 (vehicle propylene glycol 400), 1, 10, 40 or 80 mg/kg/day for 6 hours/day for 21 consecutive days (Osherhoff, 1987b). A dose-related increase in mortalities was seen in the treatment groups (2 males at 1 mg/kg/day, 2 males at 10 mg/kg/day, 3 males and 2 females at 40 mg/kg/day, 3 males and 4 females at 80 mg/kg/day). Clinical signs were observed in all of the treatment groups, including anorexia, lethargy, ataxia, hunch posture, labored respiration, soft feces, thin appearance, low body temperature and tremors. There were no significant differences in dermal irritation, body weights, food consumption, and ophthalmological findings. The surviving female at 80 mg/kg/day had reduced RBC count, hemoglobin, hematocrit, alkaline phosphatase, and gamma glutamyl transferase values and increased alanine aminotransferase, aspartate transferase and blood glucose values. Males at 80 mg/kg/day only had reduced lymphocyte values. The plasma ChE activity was reduced at 10 mg/kg/day (M: 62% of controls), 40 mg/kg/day (M: 27%; F: 42% of controls), and 80 mg/kg/day (M: 14%; F: 25% of controls). A reduction in RBC ChE activity was also observed at 10 mg/kg/day (M: 60%; F: 55% of controls), 40 mg/kg/day (M: 22%; F: 20% of controls), and 80 mg/kg/day (M: 20%; F: 24% of controls). In addition, brain ChE activity was reduced at 10 mg/kg/day (M: 58%; F: 63% of controls), 40 mg/kg/day (M: 20%; F: 24% of controls), and 80 mg/kg/day (M & F: 12% of controls).

Histological examination revealed lesions in the liver (capsular/subcapsular necrosis with acute inflammation, hepatocytic clearing, congestion, coagulation necrosis) at 10, 40 or 80 mg/kg/day, in the gallbladder (caseous necrosis, hemorrhage, chronic serosal inflammation, vasculitis, thrombosis, fibroid necrosis, granulation tissues) at 10, 40 and/or 80 mg/kg/day, in the stomach (erosion/ulceration, inflammation, hemorrhage, submucosal fibrin) in all groups, in the kidney (serous atrophy of fat) at 40 and 80 mg/kg and in the heart (degeneration of aortic media, inflammation of myocardium, myocardial degeneration) at 1, 40 and/or 80 mg/kg/day. The investigators considered the liver lesions to be compound-related; however, they suggested the gall bladder lesions were secondary to reflux of enteric bacteria into the bile duct due to episodes of hyperperistalsis. The investigators also suggested that the ulceration and inflammation in the stomach was stress-related due to the wrapping material and/or neck collar. Evidence of stress was seen in all groups, including the controls based on poor weight gains and subnormal food consumption. The investigators also attributed the serous atrophy of fat in the kidneys to the weight loss. However, the toxicological significance of the lesions in the stomach and heart were uncertain since only one stomach and no hearts from control animals were examined microscopically apparently due to protocol stipulations and the lack of gross lesions. Consequently, DPR toxicologists assumed that the lesions in the stomach and heart were treatment-related. The NOEL appears to be less than 1 mg/kg/day based on the deaths and histological lesions in the heart and stomach. One major deficiency of this study was the incomplete histopathological examination of control and high dose animals.

Dermal-Turkey

Ten 8-week-old and 10 18-week-old turkeys (sex not reported) were exposed dermally to methidathion (purity not reported) by placing them in pens in which the soil had been sprayed at 0 and 64 lb a.i./acre (Radeleff and Kunz, 1972). The birds were observed for 28 days following the spraying. Signs were not observed in any of the birds, although the 8-week-old birds at 64 lb/acre had reduced plasma ChE activity (46% of normal). This study had major deficiencies based on the FIFRA guidelines for subchronic studies, including no analysis of test article, inadequate exposure duration, inadequate number of dose levels, no overt toxicity at highest dose tested, inadequate summary of clinical signs, no pathological examination, and no individual data.

D. CHRONIC TOXICITY/ONCOGENICITY

Summary

Seven oral chronic toxicity studies were available for methidathion using four different species, including mice, rats, dogs and monkeys. Effects seen with chronic exposure were similar to those observed with subchronic exposure, although hepatotoxicity was more prevalent. In addition, focal accumulation of foamy macrophages in the alveoli and ulceration and inflammation of the skin were seen in one chronic feeding study in rats. The lowest NOEL observed in an acceptable study was 0.15 mg/kg/day based on the elevated liver enzymes in the serum and histological lesions in the liver of dogs. There was an increase in hepatocellular adenomas and carcinomas in males in two mouse studies. There was no evidence of oncogenicity in female mice or in either of the rat studies. Three of the 7 chronic toxicity studies met FIFRA guidelines.

Diet-Mouse

Sixty CD-1 mice/sex/dose were administered methidathion (98.8% purity) in the feed at 0, 1, 10, or 100 ppm (0, 0.15, 1.5 or 15 mg/kg/day, respectively[2]) for 18 and 19 months for males and females, respectively (IBT, 1980). There was no treatment-related effect on clinical signs or body weights. A significant increase in several gross pathological lesions were seen in males at 100 ppm, including liver cysts, liver nodules, and spleen nodules. Histopathological examination revealed an increase in neoplastic lesions (hepatocellular adenomas and carcinomas) and non-neoplastic lesions (cystic bile ducts, chronic pericholangitis, intracanalicular pigment, bile duct hyperplasia, and focal necrosis) in the liver of males at 100 ppm. There was no increase in neoplastic or non-neoplastic lesions in the liver of females. The NOEL for non-oncogenic systemic toxicity appears to be 10 ppm (1.5 mg/kg/day) based on the gross and histopathological changes in the liver and spleen. The study had numerous major deficiencies including no food consumption data, control group mistakenly dosed with treated feed in month 14, apparent degradation of test material in the first 8 months, and no hematology data.

Diet-Mouse

Groups of 170 CD-1 mice/sex/dose were fed methidathion technical (purity not reported) in the diet at 0, 3, 10, 50 or 100 ppm (M: 0, 0.4, 1.4, 6.7 or 13.1 mg/kg/day; F: 0, 0.5, 1.6, 8.1 or 15.9 mg/kg/day, respectively) (Goldenthal, 1986). Fifty mice/sex/dose assigned to the oncogenicity study were terminated at 23 months. The remaining 120 mice/sex/dose were assigned to the chronic toxicity study which terminated at 18 months with 4 interim sacrifices at 3, 6, 12 and 13 months. The mice sacrificed at 13 months were removed from treated feed at 12 months and then allowed to recover on the control diet for one month. An increase in mortality rate (68% versus 42% in controls) was observed in the males at 100 ppm in the oncogenicity study. Discolored urine (dark yellow, orange or red) were observed in males at 50 and 100 ppm. The cause of the discoloration is unclear, although orange or red colored urine is clearly not normal. It could be due to blood in the urine or excretion of some orange to red colored product. No other treatment-related clinical signs were seen. There were no treatment-related differences in body weights, food consumption, water consumption, auditory response, ophthalmological findings, or hematology. Significant increases in several liver enzyme activities in the serum were seen which were suggestive of hepatotoxicity. The mean serum alkaline phosphatase (AKP) activity was significantly elevated in males at 100 ppm at 3, 6, 12, 18 and 23 months (12, 4, 10, 19, and 7 fold increase, respectively). Significant increases in the mean serum alanine aminotransferase (ALT) activity were observed in males at 50 ppm (200 and 122% at 12 and 23 months, respectively) and 100 ppm (146, 149, 274, 124 and 209% at 3, 6, 12, 18 and 23 months, respectively). The mean ALT values were significantly increased in females at 100 ppm (97 and 183% at 6 and 12 months, respectively). The mean aspartate aminotransferase (AST) activity was also increased in males at 100 ppm (64, 142 and 108% at 6, 12, and 23 months, respectively). The mean plasma ChE activity was increased significantly in males at 100 ppm (27, 18, 44 and 54% of controls at 6, 12, 18 and 23 months, respectively). In contrast, the mean

---

2 Estimated assuming for a mouse that 1 ppm in the diet is equivalent to 0.15 mg/kg/day (FDA, 1959).

RBC ChE activity was significantly reduced in males at 100 ppm (55 and 62% of controls at 3 and 12 months, respectively). In females, the mean RBC ChE activity was reduced at 50 ppm (70, 64, 73, and 74% of controls at 3, 6, 18, and 23 months, respectively) and 100 ppm (55, 66, 57, 65, and 71% of controls at 3, 6, 12, 18 and 23 months, respectively). Brain ChE activity was significantly reduced at 100 ppm for both males and females (males: 61, 62, 51, 66, and 64% of controls at 3, 6, 12, 18 and 23 months, respectively; females: 77, 76, 74, 78, and 66% of controls at 3, 6, 12, 18 and 23 months, respectively).

Numerous gross pathological lesions in the liver were seen, primarily the males, including enlargement, foci, masses, nodules, cysts, discoloration, mottling, depressions, and granularity. Microscopic examination of the liver and gall bladder revealed a significant increase in numerous non-neoplastic lesions in males at 50 and 100 ppm and in females at 100 ppm (Table 4). The non-neoplastic changes included cholecystitis, hyperplasia of the gall bladder and bile duct, bile stasis, cholangiofibrosis, and chronic hepatitis.

Neoplastic lesions of the liver were also observed in males which consisted of hepatocellular adenomas and/or carcinomas (Table 5). The incidence of hepatocellular adenomas and carcinomas exhibited a dose-related trend that was highly significant when the tumors were analyzed separately or combined. In addition, 3 males at 100 ppm had multiple liver tumors. The increase in hepatocellular adenomas was significant by pairwise comparison to controls at all dose levels. The incidence of hepatocellular adenomas at 100 ppm exceeded the historical control range for this tumor type in studies conducted at the test laboratory between 1978 and 1985 with this strain of mice (Table 6) (Quest *et al.*, 1990*)*. Based on these historical control means, it appears that the incidence of adenomas in the control group in this study is unusually low. The toxicological significance of the apparent increase in adenomas at 3, 10 and 50 ppm is uncertain since the incidences are all greater than the historical control means, but within the historical control range. The increase in hepatocellular carcinomas was only significantly different ($p < 0.05$) than controls at 100 ppm. However, the incidence of carcinomas in the concurrent control group was greater than the historical control range. When combined, the increase in hepatocellular adenomas and carcinomas was statistically significant ($p < 0.05$) at 50 and 100 ppm. The incidence of carcinomas and combined adenomas/carcinomas exceeded the historical control range at 50 and 100 ppm.

Although there were no treatment-related differences in body weights, an increase in the mean liver weights was observed in males at 50 (absolute: 35%; relative to body: 36% ; relative to brain: 36%) and 100 ppm (absolute: 122%; relative to body: 116%; relative to brain: 120%) at 23 months. There was also a significant increase in the mean spleen weights (absolute: 67%; relative to body: 67%; relative to brain: 75%) and a decrease in the mean testes weights (absolute: 26%; relative to body: 29%; relative to brain: 26%) in males at 100 ppm that were sacrificed at 23 months. The increased spleen weights were associated with macroscopic changes including enlargement, nodules, adhesions and mottling of the spleen. An increase in extramedullary hematopoiesis of the spleen were observed microscopically in males at 100 ppm. No macroscopic or microscopic changes in the testes were associated with the decrease in testes weight. Significant changes in the kidney (3 ppm), brain (100 ppm) and adrenal gland weights (100 ppm) observed in females were of uncertain toxicological significance since they were not associated with pathological changes. The NOEL established for systemic non-neoplastic effects was 10 ppm (1.4 mg/kg/day) based on reduced RBC ChE activity (F: 64-74% of controls),

Table 4. Non-neoplastic Lesions in the Liver and Gall Bladder of Mice Fed Methidathion in the Diet for 23 Months[a]

Lesion	Dose (ppm)[b]				
	0	3	10	50	100
MALES					
Gallbladder Cholecystitis	4/49+++ (8%)	0/46 (0%)	1/47 (2%)	21/48*** (44%)	37/48*** (77%)
Hyperplasia	0/49+++ (0%)	0/46 (0%)	0/47 (0%)	15/48*** (31%)	33/48*** (69%)
Liver Bile duct hyperplasia	0/50+++ (0%)	1/47 (2%)	0/47 (0%)	21/49*** (43%)	42/48*** (88%)
Bile stasis	0/50+++ (0%)	0/47 (0%)	0/47 (0%)	25/49*** (51%)	47/48*** (98%)
Cholangiofibrosis	1/50+++ (2%)	0/47 (0%)	0/47 (0%)	18/49*** (37%)	45/48*** (94%)
Chronic hepatitis	3/50+++ (6%)	1/47 (2%)	2/47 (4%)	24/49*** (49%)	47/48*** (98%)
FEMALES					
Gallbladder Cholecystitis	1/45+++ (2%)	1/46 (2%)	0/46 (0%)	2/44 (5%)	11/46** (24%)
Hyperplasia	0/45+++ (0%)	0/46 (0%)	0/46 (0%)	0/44 (0%)	5/46* (11%)
Liver Bile duct hyperplasia	0/46 (0%)	1/48 (2%)	2/47 (4%)	0/44 (0%)	3/46 (7%)
Bile stasis	0/46+++ (0%)	1/48 (2%)	1/47 (2%)	0/44 (0%)	11/46*** (24%)
Cholangiofibrosis	0/46+++ (0%)	0/48 (0%)	1/47 (2%)	0/44 (0%)	7/46** (15%)
Chronic hepatitis	3/46++ (7%)	2/48 (4%)	2/47 (4%)	4/44 (9%)	8/46 (17%)

a Goldenthal, 1986
b Dose level of 0, 3, 10, 50 or 100 ppm = 0, 0.4, 1.4, 6.7 or 13.1 mg/kg/day, respectively, in males and 0, 0.5, 1.6, 8.1 or 15.9 mg/kg/day, respectively, in females
++,+++ Significant trend based on the Armitage-Cochran trend test at $p < 0.01$ and 0.001, respectively (Gart *et al.*, 1986).
*,**,*** Significantly different from the control group based on the Fisher's exact test at $p < 0.05$, 0.01 and 0.001, respectively.

Table 5. Neoplastic Lesions in the Liver of Male Mice Fed Methidathion in the Diet for 23 Months[a]

Lesion	Dose (ppm)[b]				
	0	3	10	50	100
Hepatocellular adenoma	1/46[c+++] (2%)	9/45** (20%)	7/47* (15%)	8/43* (19%)	24/45*** (53%)
Hepatocellular carcinoma	8/46[+++] (17%)	6/45 (13%)	4/47 (9%)	13/43 (30%)	17/45* (38%)
Combined[d]	9/46[+++] (20%)	15/45 (33%)	11/47 (23%)	21/43** (49%)	38/45*** (84%)

a Goldenthal, 1986
b Dose level of 0, 3, 10, 50 or 100 ppm = 0, 0.4, 1.4, 6.7 or 13.1 mg/kg/day; respectively
c The denominator is the number of animals at risk (excluding those that died before the first tumor was observed on day 445); the number in parentheses represents the incidence in percentage.
d Animals with both adenomas and carcinomas counted once under combined. There were 3 animals at 100 ppm with both adenomas and carcinomas.
+++ Significant trend based on the Armitage-Cochran trend test at $p < 0.001$ (Gart *et al.*, 1986).
*,**,*** Significantly different from the control group based on the Fisher's exact test at $p < 0.05$, 0.01 and 0.001, respectively.

Table 6. Historical Control Data on Liver Tumor in Male CD-1 Mice[a]

Type of Liver Tumor	Studies terminated between			
	1978 and 1983 (11 studies)		1984 and 1985 (3 studies)	
	Mean (%)	Range (%)	Mean (%)	Range (%)
Adenoma	11	0-26.7	14.8	8.0-24.0
Carcinoma	5.7	0-14.3	6.9	3.3-10.0
Combined	16.7	5.0-26.7	20.0	13.3-32.0

a Data obtained from 11 studies conducted at the test laboratory and terminated between 1978 and 1983, and from 3 studies conducted at the test laboratory and terminated between 1984 and 1985 (Quest *et al.*, 1990). The oncogenicity study of methidathion in CD-1 mice was terminated in 1984.

discolored urine, elevated serum ALT values, and histopathological lesions in the liver and gall bladder of males. This study was considered acceptable by DPR toxicologists based on FIFRA guidelines.

Diet-Rat

Twenty-five albino rats (strain not reported)/sex/dose were fed a 40% methidathion wettable powder (actual purity not reported) in the diet at 0, 4, 16 or 64 ppm (as active ingredient; 0, 0.2, 0.8 or 3.2 mg/kg/day, respectively[3]) for 2 years (Johnston, 1967). The body weights were reduced (25% at terminal sacrifice) in males at 64 ppm throughout the study. The mean hemoglobin level was reduced (21%) in males at week 100 due primarily to two males with very low hemoglobin values. There were no dose-related reductions in the mean plasma ChE activity, except for the females at 64 ppm which had consistently reduced activity from week 13 to 100 (66-88% of control activity). The mean RBC ChE activity was reduced at both 16 ppm (M: 55%; F: 81% of controls) and 64 ppm (M: 11%; F: 55% of controls) from week 13 to 100. A reduction in the mean brain ChE activity was seen at 4 ppm (M: 86%; F: 92% of controls), 16 ppm (M: 77%; F: 90% of controls), and 64 ppm (M: 37%; F: 33% of controls) at the terminal sacrifice. There was no effect on the absolute and relative organ weights, except for a reduction in the mean weights of the ovary in females at 64 ppm (absolute: 1%; relative: 26%) and of the adrenal glands in females at 16 ppm (absolute: 18%; relative: 13%) and 64 ppm (absolute: 32%; relative: 28%), respectively. No treatment-related differences in gross pathological findings were seen. A slightly higher incidence of degenerative changes in the liver were seen in the treatment groups than the controls; however, the study pathologist indicated that the high incidence of deaths due to pulmonary infections and subsequent autolysis made interpretation of the hepatic changes difficult. The NOEL was less than 4 ppm (0.2 mg/kg/day) based on reduced brain ChE activity (M: 86%; F: 92% of controls). The study had major deficiencies including high mortality due to pulmonary infections, insufficient hematological and clinical chemistry analysis, and incomplete histopathology and individual data.

Diet-Rat

Methidathion (97.3% purity) was administered in the feed to 80 Sprague-Dawley rats/sex/dose at 0, 4, 40 or 100 ppm (M: 0, 0.17, 1.77 or 4.95 mg/kg/day; F: 0, 0.23, 2.24 or 6.94 mg/kg/day, respectively) for 104 weeks (Yau *et al.*, 1986). There was no treatment-related effect on mortality and ophthalmological findings. An increased incidence of alopecia, chromorhinorrhea, hyperactivity, hypersensitivity to touch, skin lesions, and tremors were noted at 40 and 100 ppm. Most of the neurological signs subsided as the study progressed suggesting tolerance since the mean brain ChE activity remained severely reduced at 40 ppm (M: 49%; F: 48% of controls) and 100 ppm (M: 34%; F: 26% of controls) at the study termination. Reductions in the mean RBC ChE activity was also seen at 40 ppm (M: 78%; F: 82% of controls) and 100 ppm (M: 77%; F: 81% of controls) at the study termination. The mean serum ChE activity was only reduced at 100 ppm (M: 72%; F: 54% of controls) at the study termination. Significant reductions in the mean body weight were noted at 40 ppm (M: 3-5%

---

[3] Estimated assuming for a rat that 1 ppm in the diet is equivalent to 0.05 mg/kg/day (FDA, 1959).

wks 1-5, 7, 9-10; F: 4-6% wks 1-3) and 100 ppm (M: 4-13% wks 1-16, 72-92; F: 12-21% wks 1-104). Significant increases in the mean feed consumption was seen at 40 ppm (M: 5-14% wks 40, 48, 76, 84, 88; F: 6-16% wks 4-12, 24, 36, 44-52, 64-80, 88) and 100 ppm (M: 5-22% wks 5-7, 16-40, 48-76, 84-100; F: 7-15% wks 24, 48, 68, 84, 88). The mean water consumption was significantly reduced at 40 ppm (F: 19-32% wks 28, 44, 84) and 100 ppm (M: 15-16% wks 9, 11; F: 14-54% wks 2-3, 6, 9, 11, 20, 28-48, 56-72, 84-92).

Significant reductions in erythrocytic parameters (hemoglobin, red blood cell counts, hematocrits, mean corpuscular volume, mean corpuscular hemoglobin and mean corpuscular hemoglobin concentration) were seen primarily in females at 100 ppm, but the reductions were usually transient and less than 10%. A significant increase in the percent neutrophils and a corresponding significant reduction in the percent lymphocytes were seen in both sexes at 100 ppm. Transient increases in granulocytes, such as neutrophils, have been observed after administration of some drugs and endotoxins, but are not believed to be of any physiological consequence (Smith, 1996). An increase in granulocytes has also been associated with chronic leukemia; however, the total white blood cell counts were not significantly different at 100 ppm even though the differential counts were affected. In addition, a significant increase in the platelet counts was seen in both sexes at 100 ppm; however, an increase in platelets has not been associated with any chemical exposure (Smith, 1996). Significant differences in various serum clinical chemistry values (aspartate aminotransferase, lactate dehydrogenase, creatine phosphokinase, glucose, blood urea nitrogen, total bilirubin, cholesterol, total protein, calcium, sodium, potassium, chloride, inorganic phosphorus) were seen in both sexes primarily at 100 ppm, but occasionally at 40 ppm. These changes were usually transient and often in a direction opposite of what is normally considered toxicologically significant. However, a few clinical chemistry changes of toxicological concern were still present at the study termination in females at 100 ppm, including an increase in serum aspartate aminotransferase (71%) and serum lactate dehydrogenase (63%). Transient reductions in urine volume and increases in urinary specific gravity were seen during the first year at 40 ppm (females) and 100 ppm (both sexes), and were not considered toxicologically significant. A significant reduction in the mean liver weights were seen in females at 40 ppm (relative to body: 14%) and in both sexes at 100 ppm (males - relative to body: 17%, relative to brain: 13%; females - absolute: 31%, relative to brain: 34%) at day 364. At study termination, only the females still had significantly reduced liver weights at 40 ppm (relative to body: 27%) and 100 ppm (absolute: 18%; relative to brain: 20%). Although no histological lesions were seen in the liver, the increase in liver enzymes in the serum and the reduction in liver weights were assumed to be due to mild hepatotoxicity. Ulceration and inflammation of the skin was observed microscopically at 100 ppm which correlated with the clinical observations of skin lesions. An increased incidence of focal accumulation of foamy macrophages in the alveoli were seen at 100 ppm. No dose-related increase in tumors was seen in this study. The systemic NOEL for this study was established at 4 ppm (M: 0.17 mg/kg/day; F: 0.23 mg/kg/day) based on the clinical signs, reduced body weights and food and water consumption, reduced RBC and brain ChE activity, reduced liver weights, and skin lesions at 40 ppm. DPR toxicologists found this study to be acceptable based on FIFRA guidelines.

Diet-Dog

Three beagle dogs/sex/dose were fed a 40% wettable powder (actual purity not stated) in their diet at 0, 4, 16 or 64 ppm (as active ingredient; 0, 0.1, 0.4 or 1.6 mg/kg/day, respectively)[4] for 105 weeks (Johnston, 1967). There was no effect on clinical signs, body weights, electrocardiograms, heart rates, blood pressure, ophthalmology, and hematology. The mean serum AKP activity was increased 1 to 2-fold in dogs at 16 and 64 ppm. The mean serum AST activity was not affected, but the mean serum ALT activity was increased in a dose-related manner at 4, 16 and 64 ppm from approximately 2 to 10 fold. There was no treatment-related effect on plasma and brain ChE activity. The mean RBC ChE activity was reduced throughout the study in dogs at 64 ppm (M&F: 67-89% of controls). Dark pigmentation of the liver was seen microscopically in a few dogs at 4 ppm and all dogs at 16 and 64 ppm. Increased pigmentation of the upper nephron tubular cells of the kidney was also noted in dogs at 64 ppm. Increased extramedullary hematopoiesis of the spleen was also seen at 16 and 64 ppm. The NOEL was 4 ppm (0.1 mg/kg/day) based on the histological changes in the liver and spleen and the elevated liver enzyme activities in the serum. This study had several major deficiencies including inadequate number of animals per group, missing electrolyte balance data, inadequate histopathological examination, and no food consumption data.

Diet-Dog

Methidathion (96% purity) was administered in the feed to 4 beagle dogs/sex/dose at 0, 0.5, 2, 4, 40 or 140 ppm (M: 0, 0.02, 0.07, 0.15, 1.33 or 4.51 mg/kg/day; F: 0, 0.02, 0.07, 0.15, 1.39 or 4.90 mg/kg/day, respectively) for 1 year (Chang and Walberg, 1991). An increased incidence of salivation and wet coat on forefoot were noted at 2 ppm and higher. However, the toxicological significance of these signs is uncertain since there was no clear dose-response relationship and no significant ChE inhibition except at 140 ppm. There was no treatment-related effects on body weights or body weight gains in either sex, but there was a reduction in food consumption (17-37%) in males at 140 ppm from weeks 7 through 45. A reduction in the percent neutrophils and a corresponding increase in the percent lymphocytes was seen at 40 and 140 ppm at 3 months. In addition, there was a decrease in mean corpuscular volume at 2 and 40 ppm at the study termination. These hematological changes are of uncertain toxicological significance either because of their transient nature or lack of dose-response relationship. Moderate to marked increases in several serum liver enzyme activities, including AKP, AST, ALT, and sorbitol dehydrogenase, were seen at 40 and 140 ppm at all time points tested (Table 7). The mean γ-glutamyl transferase activity was elevated in females at 40 (40%) and 140 ppm (40-80%) at 3 and 6 months. Increases in the mean total bilirubin (100-200%) were seen in both sexes at 40 and 140 ppm at 3 months and in males at 12 months. Reductions in the mean total serum protein (8% at 6 months) and serum albumin (9-15% at 3, 6 and 12 months) were seen in females at 40 and 140 ppm. Serum ChE activity was not affected at any dose level. The mean RBC activity was reduced at 140 ppm (M: 13-23%; F: 17-24% of controls) at 3, 6 and 12 months. The mean brain ChE activity was also reduced at 140 ppm in the vermis of the cerebellum (M: 73%; F: 78% of controls) and the right hemisphere minus the vermis (M: 84%;

---

[4] Estimated assuming for a dog that 1 ppm in the diet is equivalent to 0.025 mg/kg/day (FDA, 1959).

Table 7. Dose-Related Effects on Serum Liver Enzyme Activity and Liver Pathology in Dogs Fed Methidathion for One Year[a]

	Dose Level (ppm)[b]					
	0	0.5	2	4	40	140
MALES						
Alkaline Phosphatase (U/L)	126 ± 46	122 ± 101	103 ± 41	99 ± 34	297* ± 38	371** ± 152
Asp. Aminotransferase (U/L)	23 ± 3	23 ± 3	21 ± 2	23 ± 3	29 ± 7	32* ± 4
Ala. Aminotransferase (U/L)	15 ± 4	21 ± 3	21 ± 4	40 ± 16	134** ± 37	140** ± 70
Sorbitol Dehydrogenase (U/L)	4 ± 1	6 ± 1	3 ± 1	6 ± 3	11** ± 3	13** ± 5
Liver Discoloration	0/4[++]	0/4	0/4	0/4	1/4	2/4
Cholestasis	0/4[+++]	0/4	0/4	0/4	4/4*	4/4*
FEMALES						
Alkaline Phosphatase (U/L)	152 ± 81	133 ± 66	114 ± 60	190 ± 40	353 ± 120	623* ± 467
Asp. Aminotransferase (U/L)	24 ± 2	25 ± 6	21 ± 3	22 ± 3	28 ± 6	35* ± 7
Ala. Aminotransferase (U/L)	17 ± 5	15 ± 1	15 ± 4	26 ± 7	126** ± 42	134** ± 58
Sorbitol Dehydrogenase (U/L)	5 ± 1	6 ± 2	6 ± 1	6 ± 1	13** ± 4	10* ± 3
Liver Discoloration	0/4[+++]	0/4	0/4	0/4	2/4	3/4
Cholestasis	0/4[+++]	0/4	0/4	0/4	4/4*	4/4*

a Chang and Walberg, 1991
b Dose level of 0, 0.5, 2, 4, 40 or 140 ppm = 0, 0.02, 0.07, 0.15, 1.33 or 4.51 mg/kg/day, respectively, in males and 0, 0.02, 0.07, 0.15, 1.39 or 4.90 mg/kg/day, respectively, in females
*,** Significantly different from controls based on the Fisher's exact test at $p < 0.05$ and 0.01, respectively.
++,+++ Significant trend based on the Cochran-Armitage trend test at $p < 0.01$ and 0.001, respectively.

F: 83% of controls). No treatment-related effects were seen in the urinalysis, fecal analysis, ophthalmological findings or organ weights. An increase in livers with generally dark red discoloration were observed macroscopically in both sexes at 40 and 140 ppm (Table 5). Moderate to marked cholestasis was observed microscopically in all dogs of both sexes at 40 and 140 ppm. Mild chronic inflammation of the liver was also observed at 40 ppm (M: 1/4; F: 3/4) and 140 ppm (F: 1/4). Although the incidence of liver inflammation did not show a dose-response relationship or correlate with the severity of cholestasis, the investigators considered it a treatment-related effect. The NOEL was established at 4 ppm (0.15 mg/kg/day) based on the elevated serum liver enzymes and liver pathology. This study was found acceptable by DPR toxicologists based on FIFRA guidelines.

Gavage-Monkey

Five to 7 rhesus monkeys/sex/dose were administered methidathion (purity not reported) by oral gavage at 0, 0.25 and 1 mg/kg/day 6 days/week for 23 months (Coulston and Golberg, 1971). There was no effect on clinical signs, body weights or food consumption. Hematological and clinical chemistry values were normal, except for an elevated alanine aminotransferase activity level in one male in the 1 mg/kg/day group at 22 months. A reduction in the mean plasma ChE activity was seen in the 1 mg/kg/day group at 22 months (M&F: 39% of controls). The mean RBC ChE activity was reduced at 1 mg/kg/day from 6 to 22 months (M&F: 60-76% of controls). There was no effect on brain ChE activity, or gross and histopathological findings. The NOEL was 0.25 mg/kg/day based on the reduction in plasma and RBC ChE activity. The study had major deficiencies including insufficient number of dose levels tested, lack of overt toxicity at the highest dose level, inadequate histopathological examination and no individual data.

E. GENOTOXICITY

Summary

Nine gene mutation studies for methidathion (5 reverse-mutation assays with *Salmonella typhimurium*, 1 reverse-mutation assay with *Escherichia coli*, and 3 host-mediated assays) were negative. Reverse mutation assays with *S. typhimurium* for 3 metabolites of methidathion were also negative. Positive responses were reported in a gene conversion/forward mutation assay with *Saccharomyces cerevisiae*. None of the gene mutation studies met FIFRA guidelines. Four chromosomal aberration studies were available for methidathion. There was an equivocal response in an *in vivo* sister chromatid exchange assay with Chinese hamsters and an unequivocal positive response in an *in vitro* sister chromatid exchange assay with Chinese hamster cell line V79. An *in vivo* micronucleus assay in Chinese hamster and a dominant lethal assay in mice were negative. An *in vivo* micronucleus assay for a metabolite of methidathion was also negative. Among the chromosomal aberrations tests for methidathion, only the dominant lethal assay met FIFRA guidelines. Six assays for DNA damage were available for methidathion, including 5 unscheduled DNA synthesis assays and 1 rec assay. These studies were all negative. Two of the unscheduled DNA synthesis assays met FIFRA guidelines. While the genotoxicity data for methidathion suggests that it does not act directly on DNA, it was not conclusive based on the few positive tests.

Gene Mutation

Five reverse mutation assays for methidathion using *Salmonella typhimurium* strains TA98, TA100, TA1535, TA1537, and TA1538 were submitted by the registrant. All five assays were negative, but none of the studies met FIFRA guidelines. The results for one assay were only presented in abstract form with no information about the levels tested, purity of test article or number of replicates (Lippens *et al.,* 1983). Two assays were conducted using methidathion (purity not stated) at 0, 25, 75, 225, 675 and 2025 µg/0.1 ml with and without metabolic activation in triplicate (Arni, 1980a&b). Both studies had major deficiencies including inadequate positive control for one strain, no individual plate data, and inadequate test article characterization. Two other assays tested methidathion (99.95% purity in one study; purity not reported in other) at 0, 10, 50, 100, 500, 1000 and 5000 µg/plate with and without metabolic activation (Simon and Poole, 1977; Satou *et al.*, 1979). The study conducted by Simon and Poole (1977) had several major deficiencies including no confirmatory assay, questionable positive controls for two strains, inadequate number of replicates and no individual plate data. The Satou *et al.* (1979) study also had major deficiencies including no indication of the number of replicates, no statistics, no individual plate data, inadequate test article characterization, and inadequate positive controls for several strains. There was no evidence of mutagenicity in a reverse mutation assay using *Escherichia coli* strain WP2 Hcr- where methidathion (99.95% purity) was tested at 0, 10, 50, 100, 500, 1000 and 5000 µg/plate with and without activation (Satou *et al.*, 1979). This study also had several deficiencies including no confirmatory assay, inadequate number of replicates, and no individual plate data.

Positive results were reported in a gene conversion/forward mutation assay where *Saccharomyces cerevisiae* MP-1 were exposed to methidathion (93.4% purity) at 675, 1250, 2500, 5000 or 10,000 µg/ml (Arni and Muller, 1981). It was not possible to assess the quality of the study based on the limited information that was available.

No evidence of mutagenicity was found in several host-mediated assays. In a study conducted by Simmon and Poole (1977), 6-10 male Swiss Webster mice/dose were given methidathion (purity not reported) by oral gavage either in a single dose at 0, 10, 20 or 40 mg/kg/day or in five daily doses at 0, 5, 10, or 20 mg/kg/day. *S. typhimurium* strains TA1535 and 1538 were injected intraperitoneally at the same time and then recovered from the peritoneal cavity four hours later. The study had several major deficiencies including no evidence of actual exposure of bacteria to test material, no individual plate data, and insufficient test article characterization. In a study conducted by Arni (1980c), 6 male albino mice/dose were administered methidathion (purity not reported) by oral gavage at 0, 5, 10, or 20 mg/kg/hour at 2 hours, 1 hour and immediately before injection of *S. typhimurium* strains TA98, TA100 or TA1537 into the tail vein. One hour later the animals were sacrificed and the homogenized liver assayed for mutants. This study also had major deficiencies including no evidence for actual exposure of bacteria to test material, no positive controls, no testing with TA1535, excessive mortality, no individual plate data and insufficient test article characterization. In a third study conducted by Strasser (1980), methidathion (purity not stated) was administered to 4 DBA/Bom/SPF mice/dose at 0 or 15 mg/kg by oral gavage after intraperitoneal injection of mouse lymphoma cells. The cells were harvested from the peritoneal cavity 3 days later. This study had major deficiencies including no evidence of actual exposure of cells to the test material, no positive controls, inadequate detail on cell viability or replicates, and inadequate test article characterization.

Reverse mutation assays using *S. typhimurium* for 3 metabolites of methidathion were all negative. The RH metabolite of methidathion, GS 12956 (purity not stated), was tested at 0, 10, 30, 90, 270 and 810 mg/0.1 ml with and without metabolic activation using strains TA98, TA100, TA 1535 and TA1537 (Arni, 1980d). The sulfoxide of methidathion, GS 28370 (purity not stated), was tested at 0, 25, 225, 675, and 2025 µg/0.1 ml with and without metabolic activation using strains TA98, TA100, TA1535 and TA1537 (Arni, 1980e). The sulfone of methidathion, GS 28369 (purity not stated), was also tested at 0, 15, 30, 60, 120, 240, 480, and 960 µg/0.1 ml with and without metabolic activation with strains TA98 and TA100 (Arni, 1980f).

Chromosomal Aberrations

No evidence of a dominant lethal effect was seen in a study conducted by Fritz (1976a) in which 20 male NMRI mice/dose were administered methidathion (98.4% purity) by oral gavage at 0, 15 or 45 mg/kg and subsequently mated over 6 weekly periods with 2 females per week. Signs of toxicity (deaths, ataxia, diarrhea, somnolence, and convulsions) were seen at the high dose. DPR toxicologists found this study acceptable based on FIFRA guidelines. An increase in sister chromatid exchanges was observed at 34 mg/kg in a study conducted by Hool (1980a) in which 4 Chinese hamsters/sex/dose were given methidathion (93.4% purity) by oral gavage at 0, 17, 34 or 68 mg/kg and sacrificed 24 hours later. The toxicological significance of this finding is unclear since an increase in sister chromatid exchanges was not seen at 68 mg/kg and this study had an inadequate number of animals/cells scored. In another study using Chinese hamster cell line V79, an increase in sister chromatid exchanges and cell cycle delay was seen at the highest dose levels, 40 and 80 µg/ml (Chen *et al.,* 1981). This study was only available as a published report and as a result it is unclear if the study met FIFRA guidelines. No increase in micronuclei formation were seen when methidathion (96.9% purity) was administered to 6 Chinese hamsters/sex/dose at 0, 17, 34 or 68 mg/kg twice 24 hours apart (Hool, 1980b). The hamsters were sacrificed 24 hours after the second dose. The slides from only 3 animals/sex/dose were scored. This study was also unacceptable to DPR toxicologists based on an inadequate number of animals examined and no data supporting the sacrifice time.

Hool (1980c) also conducted a micronucleus assay with the methidathion RH metabolite, GS 12956 (purity not stated), in which 3 Chinese hamsters/sex/dose were administered the test compound by oral gavage at 0, 121, 242, or 484 mg/kg/day twice 24 hours apart. The hamsters were sacrificed 24 hours after the second dose. No increase in micronuclei was found; however, DPR toxicologists found the study unacceptable due to insufficient information.

Other Genotoxic Effects

There was no evidence of mutagenicity in a rec assay in which *Bacillus subtilis* strains H17 and M45 were exposed to methidathion (99.95% purity) at 0, 250, 500, 1250, 2500, 5000 or 10000 µg/well without activation (Satou *et al.*, 1979). This study was unacceptable to DPR toxicologists based on no metabolic activation and insufficient information. Two acceptable autoradiographic DNA repair tests using primary hepatocytes from adult male Tif.FAIf(SPF) rats were negative for methidathion. In one test, cells were exposed to methidathion (97.2% purity) at 0, 0.128, 0.64, 3.2, and 16 mg/ml for 5 hours (Hertner, 1988). In the second test, cells were exposed to methidathion (96.0% purity) at 0, 1.85, 5.56, 16.67, 50, 100, and 200 mg/ml for 16-18 hours (Hertner, 1990). An autoradiographic DNA repair test was also conducted using human fibroblasts (Ciba-Geigy, 1982). Cells were exposed to methidathion (purity not stated) at 0, 1.024, 5.12, 25.6 or 128 µg/ml for 5 hours. No significant difference in the number of silver grains per nucleus were seen. This study had major deficiencies including no metabolic activation, no background grain counts, inadequate protocol information, inadequate test material information, and inadequate data summary. Two unscheduled DNA synthesis (UDS) assays were also negative for methidathion (purity not stated) using mouse and rat primary hepatocytes (Tong, 1982a&b). Hepatocytes were exposed at concentrations from 5 x 10^{-7}% to 1% (mouse) and 5 x 10^{-9}% to 1% (rat). Both were unacceptable based on insufficient information regarding the purity of the test article and number of cells examined.

Two *in vivo* studies were available in which liver DNA damage was evaluated in rats exposed to pesticide mixtures containing methidathion. In one study, the pesticide mixture induced free radical DNA damage based on an increase in the levels of 8-OH-2-deoxyguanosine in liver DNA at low doses, but not at high doses (Lodovici *et al.*, 1994). The investigators suggested the lack of free radical damage at high doses was due to a depression of cellular metabolism based on reductions in benzo(*a*)pyrene hydroxylase, *N*-demethylase activities, glutathione peroxidase, glutathione reductase, glutathione *S*-transferase and thiol transferase activities. In a medium-term liver bioassay, a significant increase in placental glutathione *S*-transferase (GST-P) positive foci was seen in the liver of rats fed a pesticide mixture containing 20 pesticides after an initial induction of hepatic carcinogenesis with diethylnitrosamine (Ito *et al.*, 1995). It is unclear if the effects seen in these studies are due to a single chemical or multiple chemicals acting either additively or synergistically. Methidathion has been shown to induce liver tumors in male mice, but not in rats.

F. REPRODUCTIVE TOXICITY

Summary

Four reproductive toxicity studies in rats were available for methidathion. Only one of these studies was found acceptable to DPR toxicologists based on FIFRA guidelines. The effects observed in the parents included tremors, alopecia, reductions in food consumption and body weights, reduced mating index and poor maternal care. The effects observed in pups included tremors, signs of maternal neglect (cool to touch, starving, weak or lethargic), reduced pup weights and reduced survival. In the one acceptable study, the parental NOEL of 5 ppm (0.4 mg/kg/day) was based on alopecia and tremors (females), reduced mating index, and poor maternal care. The reproductive NOEL in this study was also 5 ppm (0.4 mg/kg/day) based on reduced pup weights and signs of maternal neglect. There was no evidence of increased postnatal sensitivity since the parental and reproductive NOELs were the same in the two studies where both were established.

Diet-Rat

Methidathion (purity not reported) was fed to 8 male and 4 female rats (strain not reported) per dose in the diet at 0 or 50 ppm (mg/kg/day) for 3 months and then mated (FPCL, 1965). The mean litter size was smaller in the treated group, but the difference was not statistically significant. The RBC ChE activity was reduced to about 20-40% of normal. It was unclear if plasma or brain ChE activity had been measured. A NOEL could not be established for this study based on this limited information. This study was unacceptable to DPR toxicologists since it did not follow standard FIFRA protocol for this type of study and the information provided was only a summary of findings; however, it was conducted before the FIFRA guidelines existed.

Diet-Rat

A 40% wettable powder methidathion formulation was fed to 10 male and 20 female rats in the diet at 0, 4 or 32 ppm (0, 0.2 or 1.6 mg/kg/day, respectively[5]) for 3 generations (Woodard Research, 1966b). The parental generation was maintained on their assigned diet for 27-28 weeks during which time the females were mated twice to different males within their treatment group. A reduction in survival of pups at 32 ppm was the only effect reported. A tentative reproductive NOEL of 4 ppm (0.2 mg/kg/day) was identified based on the reduced survival of pups. A parental NOEL could not be identified based on insufficient information. This study had major deficiencies including no analysis of test article and diet, inadequate number of dose levels tested, inadequate number of animals per dose level, no summary of clinical signs, body weights, and food consumption, inadequate summary of reproductive parameters, inadequate pathological examination, and no individual data.

Diet-Rat

As a pilot study, a one-generation, two-litter reproductive toxicity study was conducted in which methidathion technical (purity not reported) was fed to 15 male and 30 female Charles River CD® Sprague-Dawley rats/dose at 0, 5, 50 or 100 ppm (M: 0, 0.4, 4.4 or 9.1 mg/kg/day; F: 0, 0.5, 4.9 or 10.6 mg/kg/day, respectively) for 12 weeks prior to mating (Salamon, 1986). After weaning the first litter, the females were rested two weeks and then mated again. No deaths or clinical signs were observed during the premating period. During F_{1a} lactation, dams at 50 and 100 ppm exhibited muscle tremors possibly due to their higher compound intake (0, 0.6, 5.9 or 11.4 mg/kg/day) during this period. In general, the tremors occurred early in the lactation period at 100 ppm and later in the lactation period at 50 ppm. There was a significant reduction in the mean body weights at 100 ppm in both sexes during premating (M: 8-9%; F: 8-14%) and in females during F_{1a} gestation (11-12%) and lactation (10-18%). The mean food consumption was also significantly reduced at 100 ppm in males during premating week 2 and 3 (12%) and in females during premating week 2 (12%) and F_{1a} lactation weeks 1 and 2 (26-34%). There was a significant reduction in the mean food consumption in females at 50 ppm during lactation week 2 (20%). The F_{1a} mating index was significantly reduced at 100 ppm (25%). A significant

---

5 Estimated assuming for a rat that 1 ppm in the diet is equivalent to 0.05 mg/kg/day (FDA, 1959).

reduction was seen in the percentage of F_{1a} pups surviving to days 4, 7, 14 and 21 (20.8-42.6%) at 100 ppm. The mean body weights of F_{1a} pups were significantly reduced at 50 ppm (5-25%) and 100 ppm (11-41%). Muscle tremors were also observed in 3 different litters of F_{1a} pups at 100 ppm. No structural anomalies or gross pathological lesions were seen in pups at the end of lactation. Based on the tremors and poor survival of pups at 100 ppm, this dose level was reduced to 25 ppm after the F_{1a} pups were weaned. However, because the reproductive performance of the animals at 25 ppm was significantly depressed during the F_{1b} mating period (14 of 22 mated with only 10 pregnancies; only 6 of the 10 delivered litters), the study was terminated. The parental NOEL appears to be 5 ppm (0.5 mg/kg/day) based on the tremors in dams at 50 ppm during lactation. The reproductive NOEL was also 5 ppm (0.5 mg/kg/day) based on the reduced pup weights. This study had several deficiencies, including no analysis of test article, changes in dose levels and only one generation was exposed due to early termination of study.

Diet-Rat

In the main reproductive toxicity study, 15 male and 30 female CR1:CD BR rats/dose were fed methidathion (95% purity) in the diet at 0, 5, 25 or 50 ppm (M: 0, 0.4, 2.2 or 4.3 mg/kg/day; F: 0, 0.5, 2.5 or 5.0 mg/kg/day, respectively) for two generations (Salamon, 1987). F_1 males at 50 ppm had significantly reduced mean body weights (15%) during weeks 1-8 of the premating period. The mean body weights for the F_0 and F_1 dams were significantly reduced (8-12%) at 50 ppm on lactation days 14 and 21. The mean food consumption was reduced in F_1 males at 25 ppm during week 2 (10%) and at 50 ppm during week 1-3 (11-14%). Significant reductions in the mean food consumption were also seen in F_0 dams at 50 ppm on lactation day 14 (15%) and F_1 dams at 50 ppm on lactation days 7 and 14 (19-28%). Significant increases in food consumption were also noted in F_0 dams at 50 ppm on gestation day 7 (23%) and at 25 ppm on gestation days 7 and 14 (14-19%) and lactation day 21 (42%). Tremors were observed in dams during lactation, usually the second or third week, in both generations at 25 and 50 ppm. It is not surprising that signs of maternal toxicity were only seen during lactation since feed intake was higher during this period. The average compound consumption of methidathion was nearly doubled during lactation (0, 0.75, 3.84 and 7.16 mg/kg/day) compared to the average compound consumption during premating and gestation (0, 0.45, 2.22 and 4.62 mg/kg/day, respectively). There was also evidence in the pups suggesting poor maternal care, including being cool to the touch, starving, weak or lethargic. It is also possible these effects are due to consumption of methidathion in the milk by the pups rather than neglect by the dams. However, without cross-fostering studies it is uncertain if the effects are from maternal neglect or direct consumption of the methidathion in the diet. Other effects were seen in the pups including a significant reduction in the mean number of viable pups per litter (F_2: 30%) at 50 ppm, a significant reduction in the mean pup body weights at 25 ppm (F_1: 8-15%; F_2: 3-20%) and 50 ppm (F_1: 9-30%; F_2: 3-40%) during lactation, a significant reduction in survival of pups to day 21 at 50 ppm (F_2: 34%), and a reduction in the mean absolute brain (F_2: 7-8%) and liver weights (F_2: 23-27%) at 50 ppm. Adult males had reduced mating indices at 25 ppm (F_1: 18.9%) and 50 ppm (F_1: 22%). Adult females had an increased incidence of alopecia at 25 and 50 ppm (F_0) and reduced mean relative liver weight (F_1: 9%) at 50 ppm and reduced mean absolute and relative ovary weights (F_0&F_1: 20-22%) at 50 ppm. The parental NOEL was established at 5 ppm (0.4 mg/kg/day) based on a reduction in the mating index in males and alopecia, poor maternal care and tremors in females. The reproductive NOEL was also 5 ppm (0.4 mg/kg/day) based on reduced pup weights and signs of maternal neglect in pups (cool to touch, starving, weak or lethargic). This study had some minor deviations from FIFRA guidelines (age at start of treatment, number of animals/sex/dose, time intervals for body weights, males sacrificed at the same time as females), but none invalidated the study. Therefore, DPR toxicologists found this study acceptable for fulfilling the data requirement for reproductive toxicity.

G. DEVELOPMENTAL TOXICITY

<u>Summary</u>

Five developmental toxicity studies were available for methidathion (3 rat studies and 2 rabbit studies). Systemic maternal effects included death, tremors, salivation, lacrimation, convulsions, ataxia, labored or raspy respiration, exophthalmia, miosis, chromodacryorrhea, crust around eyes, vaginal bleeding, unthriftiness, lethargy, stool alterations, loss of righting reflex, reduced food consumption and body weights. The lowest maternal NOEL in an acceptable study was 1.0 mg/kg/day based on the mortality, clinical signs, and a reduction in food consumption and body weights in pregnant rats. Fetal effects included reduced ossification of the sternabrae and reduced body weights. The lowest developmental NOEL in an acceptable study was equal to or greater than 2.5 mg/kg/day, the highest dose tested in rats. There was no evidence of increased prenatal sensitivity in any of these studies based on the developmental NOEL being equal to or greater than the maternal NOEL.

<u>Gavage-Rat</u>

Methidathion (technical, purity not reported) was administered by gavage in an aqueous solution of 2% carboxymethylcellulose to 24, 28, 23 and 21 pregnant female Sprague-Dawley rats at 0, 1, 2.5, and 5.0, respectively, on gestation days 6-15 (Fritz, 1976b). Dams at 5.0 mg/kg/day had tremors after each dosing beginning on treatment day 4. A reduction in food intake and body weights were observed in dams at 2.5 and 5.0 mg/kg/day (no means or individual data provided). Incompletely ossified 5th sternabrae were observed at 5.0 mg/kg/day. The maternal NOEL was 1 mg/kg/day based on the reduction in body weights and food consumption. The developmental NOEL was 2.5 mg/kg/day based on the reduced ossification of the sternabrae. This study had major deficiencies including no analysis of test material or dosing solution, no summary tables for body weights, food consumption, uterine weights, fetal sex, and number of corpora lutea, no gross pathological examination of dams, and no individual data.

<u>Gavage-Rat</u>

In a range-finding study, 24 pregnant female Crl:COBS CD (SD) BR rats/dose were administered methidathion (technical, purity not reported) by oral gavage at 0 (vehicle = 3% cornstarch with 0.5% Tween 80), 0.1, 1.0 or 7.5 mg/kg/day on gestation days 6-15 (Marcsinsin *et al.*, 1986). Eighteen animals at 7.5 mg/kg/day died before the end of the study. Numerous clinical signs were seen at 7.5 mg/kg/day including ataxia, chromodacryorrhea, crust around eyes, labored respiration, lacrimation, salivation, tremors, convulsions, vaginal bleeding and unthriftiness. The onset of most of these signs (except ataxia, crust around eyes, vaginal bleeding and unthriftiness) was between gestation days 6 and 9 (treatment days 1 and 4) and, therefore, these signs were considered acute effects. Significant reductions in the mean food consumption (18-70%) and body weights (15-23%) were seen in females at 7.5 mg/kg/day during treatment. There was no significant effect on reproductive parameters including the number of corpora lutea, implantation sites, resorptions or dead fetuses. A significant reduction in the mean fetal weights was seen (M:18%; F: 19%). No significant increase in gross (external) malformations was observed in the fetuses. The maternal NOEL for this study was established at 1.0 mg/kg/day based on the mortalities, clinical signs and reduction in food consumption and body weights. The developmental NOEL was also 1.0 mg/kg/day based on the reduced fetal body weights. This study had several major deficiencies including no analysis of test article or dosing material, and no microscopic examination of fetuses for skeletal or visceral malformations.

Gavage-Rat

Methidathion (95% purity) was administered by oral gavage to 25 pregnant female Crl:COBS CD (SD) BR rats/dose at 0 (vehicle = 3% cornstarch with 0.5% Tween 80), 0.25, 1.0 or 2.5 mg/kg/day on gestation days 6-15 (Mainiero *et al.*, 1987). One animal at 2.5 mg/kg/day died on gestation day 12. Clinical signs were observed in dams at 2.5 mg/kg including lethargy, tremors, salivation, lacrimation, exophthalmia, raspy respiration, vaginal bleeding, and chromodacryorrhea. The onset of some of these signs (lethargy, tremors, salivation and raspy respiration) was between gestation days 6 and 9 (treatment days 1 and 4) and, therefore, the signs were considered acute effects. Significant reductions in the mean food consumption (9-16%) and body weights (5%) were seen at 2.5 mg/kg/day. There was no treatment-related effect on pregnancy rate, number of corpora lutea, resorptions, or stillbirths, sex ratio, fetal weights or fetal malformations (gross, visceral or skeletal). The maternal NOEL was established at 1.0 mg/kg/day based on the mortality, clinical signs, and reduction in food consumption and body weights. The developmental NOEL was equal to or greater than 2.5 mg/kg/day, the highest dose tested. DPR toxicologists found this study acceptable based on FIFRA guidelines.

Gavage-Rabbit

Six pregnant New Zealand White were administered methidathion (purity not reported) by oral gavage at 0 (vehicle = 3% cornstarch solution with 0.5% Tween 80), 10, 30 and 50 mg/kg/day on gestation days 7-19 (Wallace, 1986). All animals at 30 and 50 mg/kg/day died during the treatment period. One doe died at 10 mg/kg/day on gestation day 15. Prior to dying, the females exhibited various signs including tremors, ataxia, salivation, miosis, lethargy, stool alterations (decreased/no/soft stools), loss of righting reflex, rales and convulsions. The food consumption was unaffected in animals at 10 mg/kg/day, but their mean body weight gains were reduced (38%) compared to controls. The only clinical sign exhibited in females at 10 mg/kg/day was stool alterations. There was no treatment related effect on reproductive parameters (pregnancy rate, number of corpora lutea, implantations, resorptions or still births) or fetal weights. The maternal NOEL was less than 10 mg/kg/day based on the death, reduced body weight gains and stool alterations. The developmental NOEL could not be established since fetuses were not examined for malformations (gross, visceral or skeletal). This study had major deficiencies primarily due to it being a dose range-finding study and, consequently, there was limited data collected and/or reported.

Gavage-Rabbit

Methidathion (95% purity) was administered by oral gavage to 19 pregnant New Zealand White rabbits/dose at 0 (vehicle = 3% cornstarch with 0.5% Tween 80), 2, 6 or 12 mg/kg/day on gestation days 7 to 19 (Hummel *et al.*, 1987). One animal at 6 mg/kg/day died on day 17 after a mis-dosing and another animal at 12 mg/kg/day was sacrificed after a back injury. Three other does (one each at 2, 6 and 12 mg/kg/day) were sacrificed early because they aborted early. Clinical signs were observed at 12 mg/kg/day including ataxia, salivation, tremors, miosis, and blood in the cage pan. There were no treatment-related changes in the maternal food consumption, maternal body weights, pregnancy rate, number of corpora lutea, implantation sites or resorptions, sex ratio of fetuses, fetal body weights or fetal malformations (gross, visceral or skeletal). The maternal NOEL was established at 6 mg/kg/day based on the clinical signs. The developmental NOEL was equal to or greater than 12 mg/kg/day, the highest dose tested. This study was acceptable based on FIFRA guidelines.

H. NEUROTOXICITY

Summary

Eight neurotoxicity studies were available for methidathion (5 acute studies in hens, 2 acute studies in rats and a 90-day study in rats). Three of these studies met FIFRA guidelines, including 1 hen study, 1 acute study in rats, and the 90-day study in rats. There was no evidence of delayed neuropathy in any of the hen studies. In the acute and subchronic neurotoxicity studies in rats, signs of neurotoxicity were observed in the functional observational battery, including changes in autonomic signs, CNS signs, sensorimotor effects, impaired neuromuscular functions and reduced body temperature. A reduction in maze activity was also observed. A reduction in ChE activity in four different regions of the brain (cerebellum, cerebral cortex with hippocampus, and striatum) and the spinal cord were seen. The acute NOEL was less than 1 mg/kg based on reduced ChE activity in the cerebral cortex of males (59% of controls) at the time of peak effect. The subchronic NOEL was 3 ppm (M: 0.182 mg/kg/day; F: 0.198 mg/kg/day) based on the reduced ChE activity in RBCs (M: 74-81%: F: 56-75% of controls - wks 4-13), cerebral cortex (M: 74% of controls - wks 2-4) and striatum (F: 63% of controls - wk 13).

Acute

Gavage-Hen

Methidathion (technical, purity not reported) was administered by gavage in 2% carboxymethylcellulose at 0 mg/kg to 10 hens (White Leghorn), 43.75 mg/kg to 15 hens, 87.5 mg/kg to 15 hens, 175 mg/kg to 30 hens and 350 mg/kg to 30 hens twice with a 21 day interval between dosing (Ullman, no date). Hens at 350 mg/kg were pretreated with atropine before dosing. Deaths occurred primarily at 175 and 350 mg/kg, but one death occurred at both 43.75 and 87.5 mg/kg. Clinical signs were seen at all treatment levels during the 42-day observation period including ataxia, convulsions, curved position, and sedation. There was no evidence of delayed neuropathy when the spinal cord and peripheral nerve were examined microscopically.

This study had several major deficiencies including no forced motor activity, no body weight data, and no histopathological examination of the thoracic spinal cord or medulla oblongata.

Gavage-Hen

Four hens (Rhode Island/Light Sussex and White Leghorn/Light Sussex hybrids) were administered 4 weekly subcutaneous injections of methidathion (purity not reported) in glycerol formal at 50 mg/kg (Geigy, 1964). Signs of acute toxicity (no details provided) were seen, but no evidence of delayed neurotoxicity (ataxia, paralysis, loss of weight) was observed. This study had numerous major deficiencies including inadequate description of methods, no analysis of test article, inadequate number of animals, no dose justification, no positive or negative control groups, no data summaries or individual data.

Gavage-Hen

Four hens (strain not reported) were given four weekly subcutaneous injections of methidathion (technical, purity not reported) in glycerol formal at 0 or 50 mg/kg (FPCL, 1965). No hens developed signs of delayed neuropathy during the 8 weeks of observation. This study had numerous major deficiencies including inadequate description of methods, no analysis of test article, inadequate number of animals, no dose justification, no positive or negative control groups, no data summaries or individual data.

Gavage-Hen

Sixty production red breed hens were administered methidathion (96.5% purity) in corn oil by gavage at 145 mg/kg twice with a 21-day interval between doses (Kuhn, 1989f). The hens were given atropine at 5, 20.5, 25.5 and 29 hours after dosing. A negative control group containing 10 hens received corn oil only. A positive control group containing 8 hens was given tri-*O*-tolyl phosphate (TOTP) at 500 mg/ml once. Twenty-eight hens receiving methidathion died, 22 after the first dose and 6 after the second dose. Eight hens receiving methidathion exhibited signs of unsteadiness after the first dose, but only one was persistent. No signs of delayed neurotoxicity were seen after the second dose. Histopathological examination of the nervous tissue did not reveal any lesions in hens receiving methidathion that were consistent with organophosphate-induced delayed neuropathy. All hens receiving TOTP exhibited ataxia by day 16 and had some degree of degeneration and swelling of the axons of some portion of the nervous tissue examined microscopically. DPR toxicologists found this study acceptable based on FIFRA guidelines.

Diet-Hen

Methidathion in a 40% wettable powder was fed in the diet to 10 hens/dose at 0, 16, 52, or 160 ppm (as active ingredient) for 45 days (Woodard Research, 1965). Hens at 160 ppm had reduced food consumption (no data provided). Discolored livers were noted in all hens receiving methidathion with a higher frequency at 160 ppm. Two hens at 160 ppm had equivocal histopathological lesion in the nerves (no details provided). This study had major deficiencies including inadequate description of methods, no analysis of test article, no data summaries or individual data.

Gavage-Rat

In a range-finding study, 3 male Sprague-Dawley Crl:CD® BR rats/dose were administered a single dose of methidathion (94.3% purity) by oral gavage at 0, 4, 8, 12, 16 or 20 mg/kg (Leahy, 1993). Three females/dose were administered methidathion at 0, 4, 16, 20 (6 females) or 30 mg/kg. An additional 5 males and 6 females were also administered methidathion at 25 mg/kg and observed for mortality for 2 days. Animals were evaluated in an abbreviated functional observational battery (FOB) at 1, 2, 3, 4, 6, and 8 hours. The effects seen included cholinergic signs (lacrimation, salivation, diarrhea, tremors, ataxia, and muscle fasciculations), central nervous system (CNS) signs, autonomic signs, neuromuscular signs, and disturbances in equilibrium at ≥ 8 mg/kg in males and ≥ 16 mg/kg in females. The onset of signs was as early as 1 hour after dosing. Deaths occurred at ≥ 20 mg/kg in males and ≥ 25 mg/kg in females. The NOEL was 4 mg/kg in both sexes based on the effects seen in the FOB. As a range finding study, this study was not designed to meet FIFRA guidelines and, therefore, it had several deficiencies including an inadequate number of animals per dose level, inadequate FOB and no pathological examination of rats.

Gavage-Rat

Methidathion (93.2%) was administered to 20 Crl:CD® Sprague-Dawley rats/sex/dose at 0, 1, 4, 8 and 16 mg/kg after an 18-hour fast (Chang and Richter, 1994). Ten animals/sex/dose were used for cholinesterase measurements at the time of peak effect (1.5 hours after dosing). A positive control group of 10 rats/sex was administered carbaryl at 30 mg/kg by gavage. No deaths occurred; however, clinical signs (muscle fasciculations, pallor, reduced activity, salivation and tremors) were observed at 8 and 16 mg/kg on the day of dosing. One female at 1 mg/kg also exhibited clinical signs, but was considered improperly dosed. There was a significant reduction in the mean cumulative body weight gain (15%) in males at 16 mg/kg. The mean food consumption was also reduced at 16 mg/kg (M: 15%; F: 11%) the first week after dosing. Significant differences were observed in both sexes in the functional observational battery (FOB) at 8 and/or 16 mg/kg (Table 8) at the time of peak effect (1.5 hours after exposure). These differences included changes in autonomic signs, CNS signs, sensorimotor effects, impaired neuromuscular functions and reduced body temperature. Some CNS signs and impaired neuromuscular function were seen in females at 1 and 4 mg/kg, but the incidence was not statistically significant. There was a significant reduction in the mean total session activity for both sexes in the figure-8 maze at 8 mg/kg (M: 62%; F: 63%) and 16 mg/kg (M: 84%; F: 83%) at the time of peak effect. There was also a significant reduction in the mean activity for females at 4 mg/kg during the first 5 minutes of measurement which the investigators considered treatment-related.

The mean serum ChE activity was reduced in males at 8 mg/kg and 16 mg/kg at the time of peak effect, but had returned to control levels two weeks after dosing (Table 9). Reductions in the mean serum ChE activity between 71% and 77% of control activity was seen in the females at all dose levels at the time of peak effect, but the reductions were not statistically significant. The mean RBC ChE activity was significantly reduced at 4, 8, and 16 mg/kg at the time of peak effect. Two weeks later, only the males at 4 mg/kg had a significant reduction in RBC ChE activity. ChE activity was measured in three different regions of the brain: cerebellum, cerebral cortex with hippocampus, and striatum. The mean ChE activity in the

Table 8. Neurological Effects in Rats Administered a Single Oral Dose of Methidathion[a]

Functional Domain/ Observations	Dose Level (mg/kg)									
	MALES					FEMALES				
	0	1	4	8	16	0	1	4	8	16
Autonomic										
Respiration	0	0	0	2	7**	0	0	0	4**	10**
Lacrimation	0	0	0	1	3	0	0	0	1	3
Salivation	0	0	0	1	2	0	0	0	0	4*
CNS Excitability										
Tremors (Home Cage)	0	0	0	3	7**	0	0	0	6**	10**
(Open Field)	0	0	0	7**	7**	0	0	0	7**	10**
Tonic Convulsions (Home Cage)	0	0	0	0	1	0	0	0	0	0
Clonic Convulsions (Open Field)	0	0	0	0	0	0	0	0	0	3
Ease of Handling (In Hand)	0	0	0	0	3	0	0	0	1	3
Ease of Removal (From Cage)	0	0	0	0	0	0	1	1	1	5*
Lowered Arousal	0	0	0	4	7**	0	1	0	3	10**
Bizarre Behavior (Home Cage)	0	0	0	4*	7**	0	1	1	5*	10**
(Open Field)	0	0	0	7**	7**	0	1	2	6**	10**
CNS Activity										
Home Cage Posture	0	0	0	2	4	0	0	0	1	5
Mean No. Rears/2 minutes	9	7	11	2**	2**	12	10	8	5**	1**
Sensorimotor										
Touch Response	0	0	0	0	4**	0	0	0	2	5**
Pupil Response	0	0	1	2	1	0	0	1	0	3
Tail Pinch Response	0	0	0	2	3	0	0	0	1	5**
Neuromuscular										
Ataxic Gait	0	0	0	8**	5**	0	2	1	8**	10**
Abnormal Gait	0	0	0	8**	7**	1	2	2	7**	10**
Righting Reflex	0	0	0	5**	6**	0	2	3	4	9**
Hindlimb Extensor Strength	0	0	0	1	2	0	1	1	2	7**
Hindlimb Position	0	0	0	2	4*	0	0	1	3	8**
Hindlimb Splay (% Control)	100	105	112	118	125*	100	119	121	128	124
Forelimb Grip Strength (% Control)	100	98	97	74*	37**	100	85	87	53**	21**
Hindlimb Grip Strength (% Control)	100	115	101	95	78	100	93	95	81	70
Physiological										
Temperature (% Control)	100	100	100	96**	96**	100	99	99	94**	92**

a Behavioral effects observed at peak time to effect, 1.5 hours after dosing. Ten animals/sex/dose at all doses except at 16 mg/kg (8 males, 9 females).

*, ** Significantly different at $p < 0.05$ & 0.01, respectively, when compared to control based on Fisher's exact test (categorical or incidence data) or Dunnett's test (quantitative or ranked data).

Table 9. Cholinesterase Activity Relative to Controls in Blood and Nervous Tissue of Rats Administered a Single Dose of Methidathion by Oral Gavage[a]

Tissue	Time	Dose Level (mg/kg)			
		1	4	8	16
MALES					
Serum	1.5 hrs	101[b]	81	70**	59**
	2 wks	116	111	129	110
Red Blood Cell	1.5 hrs	97	42**	26**	16**
	2 wks	102	65*	82	73
Cerebellum	1.5 hrs	88	47**	32**	22**
	2 wks	97	98	93	84
Cerebral Cortex w/ Hippocampus	1.5 hrs	59**	32**	12**	6**
	2 wks	129	130	104	95
Striatum	1.5 hrs	107	28**	16**	9**
	2 wks	110	135	68	64
FEMALES					
Serum	1.5 hrs	77	76	77	71
	2 wks	92	101	112	108
Red Blood Cell	1.5 hrs	91	33**	18**	14**
	2 wks	94	93	78	81
Cerebellum	1.5 hrs	87	39**	25**	17**
	2 wks	95	95	92	91
Cerebral Cortex w/ Hippocampus	1.5 hrs	87	29**	11**	6**
	2 wks	98	102	91	85
Striatum	1.5 hrs	92	27**	8**	5**
	2 wks	233	117	187	140

a Chang and Richter, 1994
b Percent of control activity
*, ** The mean activity was significantly different from controls by Dunnett's test at $p < 0.05$ and 0.01, respectively.

cerebellum was significantly reduced at 4, 8, and 16 mg/kg. Significant reductions in the mean ChE activity in the cerebral cortex were seen at 1.5 hours after dosing at 1 (males only), 4, 8 and 16 mg/kg. The mean ChE activity in the striatum was also significantly reduced at the time to peak effect at 4, 8, and 16 mg/kg. The mean ChE activity in all three brain regions had returned to control levels by two weeks, except for the striatum where reductions in the mean activity were still present in males at 8 and 16 mg/kg. However, the reductions in the ChE activity in the striatum at 2 weeks were not statistically significant. There is some uncertainty about the toxicological significance of the ChE inhibition in the cerebral cortex of males at 1 mg/kg since the females appear to be more sensitive to methidathion based on the higher incidence of effects in the FOB and the more severe reduction in ChE activity in all three regions of the brain at higher dose levels. Furthermore, the cerebral cortex does not appear to be uniquely sensitive to ChE inhibition when compared to the striatum at 4 mg/kg and higher. It is also unusual to see significant brain ChE inhibition without either serum or RBC ChE inhibition. However, the reduction in cortex ChE activity at 1 mg/kg does not appear to be a statistical aberration based on similar reduction in ChE activity in this brain region of males at 10 ppm (0.6 mg/kg/day) in a 90-day neurotoxicity study (Chow and Turnier, 1995). Therefore, DPR toxicologists made a health protective assumption that the ChE inhibition in the cerebral cortex of males at 1 mg/kg was of toxicological significance. No treatment-related gross or histopathological lesions were found. The study LOEL was 1 mg/kg/day based on the reduced ChE activity (59% of controls) in the cerebral cortex of males at 1.5 hours after exposure and, therefore, the NOEL was less than 1 mg/kg/day. DPR toxicologists found this study acceptable based on FIFRA guidelines.

Subchronic

Diet-Rat

Groups of 30 Crl:CD® Sprague-Dawley rats/sex/dose were fed methidathion (94.9% purity) at 0, 3, 10, 30 or 100 ppm (M: 0, 0.182, 0.608, 1.86 or 6.36 mg/kg/day; F: 0, 0.198, 0.659, 2.01 or 7.19 mg/kg/day, respectively) for 90 days (Chow and Turnier, 1995). Ten rats/sex were administered acrylamide at 16 mg/kg by oral gavage as a positive control group. Two males at 10 ppm and 1 male at 30 ppm died during the study; however, the investigators did not consider any of these deaths to be treatment-related. Treatment-related clinical signs were seen in females at 100 ppm, including infrequent stools, transient tremors, and chromorhinorrhea. Females at 100 ppm had a dramatic reduction in body weight gains during the first two weeks of the study (67% and 36%, respectively) which resulted in the mean cumulative body weight gain to be significantly reduced until the near end of the study (16% at week 12). There was no significant reduction in the food consumption in females to account for the dramatic reduction in body weights during the first two weeks. The only treatment-related effects seen in the FOB were in females at 100 ppm. These effects included neuromuscular effects (abnormal gait and reduced forelimb and hindlimb grip strength), CNS signs (tremors, stereotypy, bizarre behavior), and sensorimotor effects (increased response to touch, sound and tail pinch). There was no significant difference in the figure-8 maze activity in either sex at any dose level.

The mean serum ChE activity was significantly reduced at 30 (females only) and 100 ppm (Tables 10 and 11). Significant reductions in the mean RBC ChE activity were seen at 10, 30, and 100 ppm. ChE activity was measured in the spinal cord and four regions of the brain: cerebellum, cerebral cortex, striatum, and hippocampus. The mean ChE activity in the

Table 10. Cholinesterase Activity Relative to Controls in Blood and Nervous Tissue of Male Rats Fed Methidathion in the Diet for 90 Days[a]

Tissue	Time	Dose Level (ppm)			
		3	10	30	100
Serum	2 wks	89[b]	76	84	65*
	4 wks	94	105	95	66
	8 wks	92	79	95	70
	13 wks	92	90	106	68*
Red Blood Cell	2 wks	99	86	66**	19**
	4 wks	93	81*	40**	10**
	8 wks	85	74**	37**	17**
	13 wks	89	80*	41**	12**
Cerebellum	2 wks	93	93	90	58**
	4 wks	96	96	87**	47**
	8 wks	102	100	88	49**
	13 wks	99	86	86	48**
Cerebral Cortex	2 wks	89	74*	78	32**
	4 wks	86	74**	56**	15**
	8 wks	115	74	66	23**
	13 wks	81	75	59*	19**
Striatum	2 wks	104	113	91	35**
	4 wks	89	98	84	16**
	8 wks	114	90	61**	17**
	13 wks	93	90	59**	13**
Hippocampus	2 wks	97	101	108	41**
	4 wks	96	97	81**	23**
	8 wks	89	97	68**	21**
	13 wks	105	96	76**	26**
Spinal Cord	2 wks	103	90	88	48**
	4 wks	123	116	98	36**
	8 wks	104	94	80	35**
	13 wks	86	87	77*	23**

a Chow and Turnier, 1995
b Dose level of 0, 3, 10, 30 or 100 ppm = 0, 0.182, 0.608, 1.86 or 6.36 mg/kg/day, respectively
c Percent of control activity
*, ** The mean activity was significantly different from controls by Dunnett's test at $p < 0.05$ and 0.01, respectively.

Table 11. Cholinesterase Activity Relative to Controls in Blood and Nervous Tissue of Female Rats Fed Methidathion in the Diet for 90 Days[a]

Tissue	Time	Dose Level (ppm)[b]			
		3	10	30	100
Serum	2 wks	138*[c]	103	136*	77
	4 wks	87	75	59**	44**
	8 wks	99	141	87	71
	13 wks	76	93	91	55*
Red Blood Cell	2 wks	95	92	54**	15**
	4 wks	87	75**	24**	9**
	8 wks	106	56**	20**	14**
	13 wks	98	68**	28**	9**
Cerebellum	2 wks	98	94	79**	41**
	4 wks	103	100	68**	34**
	8 wks	102	82	80	20**
	13 wks	92	81	64**	32**
Cerebral Cortex	2 wks	97	99	60**	18**
	4 wks	88	86	41**	11**
	8 wks	104	102	37**	11**
	13 wks	95	85	34**	8**
Striatum	2 wks	92	91	56**	9**
	4 wks	105	96	34**	6**
	8 wks	100	88	31**	3**
	13 wks	95	63**	34**	4**
Hippocampus	2 wks	97	89	60**	17**
	4 wks	105	97	71**	13**
	8 wks	102	83	32**	7**
	13 wks	103	76**	44**	9**
Spinal Cord	2 wks	102	103	72**	30**
	4 wks	116	93	52**	19**
	8 wks	102	86	47**	18**
	13 wks	108	99	64**	17**

a Chow and Turnier, 1995
b Dose Level of 0, 3, 10, 30 or 100 ppm = 0, 0.198, 0.659, 2.01 or 7.19 mg/kg/day, respectively
c Percent of control activity
*, ** The mean activity was significantly different from controls by Dunnett's test at $p < 0.05$ and 0.01, respectively.

cerebellum was significantly reduced at 30 and 100 ppm. In the cerebral cortex, significant reductions in the mean ChE activity were observed at 10 (males only), 30 and 100 ppm. There was some uncertainty about the toxicological significance of the reduced ChE activity in the cerebral cortex of males at 10 ppm because females had more pronounced inhibition of ChE in this region at higher doses. Furthermore, males did not exhibit any abnormal behavior in the FOB or maze even at 100 ppm. However, the cortex ChE activity in males at 10 ppm was consistently reduced to about 75% of control activity throughout the study (although it was not always statistically significant). Therefore, DPR toxicologists made the health protective assumption that the ChE inhibition in males at 10 ppm was of toxicological significance. The mean ChE activity in the striatum was reduced at 10 (females only), 30, and 100 ppm. Significant reductions in the mean ChE activity were seen in the hippocampus at 30 and 100 ppm. The mean ChE activity in the spinal cord was also significantly reduced at 30 and 100 ppm. No treatment-related gross or histopathological lesions were found. The NOEL for this study was established at 3 ppm (M: 0.182 mg/kg/day; F: 0.198 mg/kg/day) based on the reduced ChE activity in RBCs (M: 74-81%; F: 56-75% of controls - wks 4-13), cerebral cortex (M: 74% of controls - wks 2-4), striatum (F: 63% of controls - wk 13), and hippocampus (F: 76% of controls - wk 13). DPR toxicologists found this study acceptable based on FIFRA guidelines.

III. RISK ASSESSMENT

A. HAZARD IDENTIFICATION

Acute Toxicity

The adverse effects observed with the acute studies are summarized in Table 12. In general, the effects that are considered adverse include clinical signs, reductions in body weight and food consumption greater than 10%, and increases in gross and histopathological lesions. Minimal changes in clinical chemistry and hematology values and organ weights without accompanying functional or structural changes are generally not considered adverse. Possible acute effects from methidathion included effects seen in the LD_{50}/LC_{50} studies, an acute neurotoxicity study, and some findings in the developmental toxicity studies. The effects observed in the LD_{50}/LC_{50} studies included dizziness, ataxia, irregular and increased respiration, dyspnea, fasciculations, trembling, salivation, exophthalmos, and death. There was insufficient information available from the LD_{50}/LC_{50} studies to establish NOELs for these effects.

In general, DPR considers brain ChE inhibition to be indicative of overt toxicity since it is one of the primary functional target sites and more subtle central neurological signs, such as memory and learning losses, may not be easily detected in animals unless they are specifically tested for these effects. The toxicological significance of plasma and RBC ChE inhibition is less certain because the physiological function of ChEs in blood have not been clearly established, although several possible physiological functions have been proposed. Plasma ChE, or more specifically butyrylcholinesterase (BuChE), may be involved in the binding/metabolism of certain drugs, such as succinylcholine, which suggests that its inhibition may compromise an organism's ability to defend against subsequent toxic insults (Lockridge and Masson, 2000). BuChE is also the predominant form of ChE in the developing nervous system of birds and mammals (Brimijoin and Koenigsberger, 1999). Other evidence suggests that BuChE may also play a role in the co-regulation of ACh levels in the adult nervous system including 1) substrate inhibition of acetylcholinesterase (AChE) at high ACh concentrations, 2) the survival of AChE knockout mice, and 3) the increase in BuChE levels in Alzheimer's disease as AChE levels decrease (Giacobini, 2003; Li *et al.*, 2000; Ballard and Perry, 2003). Due to the expression of AChE in several types of hematopoietic cell lines, it has been proposed that circulating AChE may be important in erythropoiesis (Grisaru *et al.* 1999). U.S. EPA does not consider plasma or RBC ChE inhibition an adverse effect in itself, but does use RBC ChE inhibition as a surrogate for peripheral ChE inhibition (U.S. EPA, 2000a). The Joint Meeting on Pesticide Residues of the FAO/WHO concluded only RBC ChE activity at the time of peak effect with acute exposure should be used as a surrogate for peripheral ChE activity (JMPR, 1999) since RBCs lack the ability to synthesize new AChE (Brimijoin, 1992). Consequently, the recovery of RBC ChE activity is much slower than in neurological and neuromuscular tissue because it is dependent on the replacement of RBCs. DPR is reevaluating the use of ChE inhibition data in its risk assessments. In anticipation of changes in the use of these endpoints in the risk assessments, NOELs for blood and brain inhibition were identified in this document based on statistical significance.

Table 12. Acute Effects of Methidathion and Their Respective NOELs and LOELs

Species	Exposure	Effect	NOEL (mg/kg)	LOEL (mg/kg)	Ref.[a]
		Oral			
Rat[b]	**Single, gavage**	**Reduced ChE[d] activity in the cerebral cortex (M: 59%)[e]**	**(0.3)[c]**	**1.0**	**1***
Rat[f]	9 days, gavage	Maternal: Tremors (onset day 4) Fetal: Reduced ossification	2.5 2.5	5.0 5.0	2
Rat[f]	9 Days, gavage	Maternal: Tremors, salivation, lacrimation, convulsions, labored respiration, chromodacryorrhea (onset days 1-4) Fetal: Reduced birth weight	1.0 1.0	7.5 7.5	3
Rat[f]	9 Days, gavage	Maternal: Lethargy, tremors, salivation, raspy respiration (onset days 1-4)	1.0	2.5	4*

a References: 1. Chang and Richter, 1994; 2. Fritz, 1976b; 3. Marcsinsin *et al.* 1986; 4. Mainiero *et al.*, 1987.
b Neurotoxicity study
c Estimated NOEL by dividing LOEL by an uncertainty factor of 3.
d ChE = Cholinesterase
e Percent of control activity
f Developmental toxicity study: All fetal effects were considered acute effects; however, only maternal effects observed within the first few days of exposure were considered acute exposure.
* Acceptable study based on FIFRA guidelines

The effects observed in the developmental toxicity studies which were considered acute included maternal signs observed within the first few days of exposure and any fetal effects assuming they were the result of a single exposure. Cholinergic signs (tremors, salivation, lacrimation, labored or raspy respiration, convulsions) were seen in dams in several developmental toxicity studies during the first few days of treatment. The NOELs in these studies ranged from 1 to 2.5 mg/kg. A NOEL of 1 mg/kg was established in an acceptable study conducted by Mainiero *et al.* (1986) where lethargy, tremors, salivation, and raspy respiration were observed in pregnant rats at 2.5 mg/kg on days 1 to 4 of treatment. Fetal effects were also observed in two of these developmental toxicity studies in rats, including reduced ossification and reduced body weights (Fritz, 1976b; Marcsinsin *et al.* 1986). The NOELs for the fetal effects were same as the maternal NOELs, 1 to 2.5 mg/kg.

In an acute neurotoxicity study in rats, treatment-related differences in clinical signs (muscle fasciculations, pallor, reduced activity, salivation and tremors), the functional observational battery (FOB) parameters and figure-8 maze activity, were seen in both sexes at 8 and 16 mg/kg at the time of peak effect (Chang and Richter, 1994). The effects seen in the FOB included autonomic signs (impaired respiration, lacrimation, salivation), CNS signs (tremors, reduced arousal, decreased activity, convulsions, muscle fasciculations, repeated opening and closing of mouth), sensorimotor effects (reduced touch and tail pinch responses), impaired neuromuscular function (ataxic and/or abnormal gait, impaired righting reflex, reduced hind limb extensor strength, reduced forelimb and hindlimb grip strength) and reduced body temperature. Some signs indicative of CNS excitability and impaired neuromuscular function were seen in females at 1 and 4 mg/kg, but the incidence was not statistically significant. The toxicological significance of the low incidence of these signs at these lower dose levels is uncertain given that there was no significant ChE inhibition in the plasma, RBCs or brain of females at 1 mg/kg. Furthermore, the incidence of these signs were not significantly greater at 4 mg/kg where there was a marked reduction in brain and RBC ChE activity (25-40% of control activity). There was a significant reduction in the mean ChE activity in the cerebral cortex of males (59% of controls) at 1 mg/kg at 1.5 hours after dosing even though there were no neurological signs observed in males at 1 or 4 mg/kg (except one male at 4 mg/kg with impaired pupil response). The toxicological significance of the ChE inhibition in the cortex of males at 1 mg/kg is uncertain for several reasons. First, the females appear to be more sensitive to methidathion based on the ChE activity in all three regions of the brain at higher dose levels and the higher incidence of effects seen in the FOB. Second, the cerebral cortex does not appear to be uniquely sensitive to ChE inhibition when compared to the striatum at 4 mg/kg and higher dose levels. Third, it is unusual to see significant brain ChE inhibition without either significant plasma or RBC ChE inhibition. However, the reduction in cortex ChE activity in males at 1 mg/kg does not appear to be a statistical aberration since a similar reduction in cortex ChE activity was seen in males at 10 ppm (0.6 mg/kg/day) in a 90-day neurotoxicity study for methidathion (Chow and Turnier, 1995). Consequently, DPR toxicologists made a health protective assumption that the ChE inhibition in the cerebral cortex of males at 1 mg/kg was of toxicological significance.

The acute neurotoxicity study was selected as the definitive study for evaluating acute dietary, drinking water, occupational and ambient air exposure to methidathion because the neurological effects were evaluated more thoroughly and the effects seen were clearly the result of a single exposure. The acute NOEL was estimated for this study by dividing the LOEL by an uncertainty factor of 3. A smaller uncertainty was used to estimate the NOEL because the severity of the endpoint was considered mild for the following reasons: 1) no significant blood ChE inhibition was seen at the LOEL; 2) only one region of the brain in one sex was affected at the LOEL; 3) the cortex was not uniquely sensitive to ChE inhibition at higher doses; 4) statistically significant increases in neurological signs were not observed in the functional observational battery in either sex until 8 mg/kg; and 5) males were not more sensitive than females based on neurological signs and regional brain ChE inhibition at higher dose levels. Furthermore, a NOEL of 0.2 mg/kg/day was observed for the same endpoint in the 90-day subchronic neurotoxicity study for methidathion. Therefore, the critical NOEL for acute effects from methidathion was estimated to be 0.3 mg/kg based on the reduced ChE activity in the cerebral cortex of males (59% of controls).

<u>Subchronic Toxicity</u>

The effects observed in laboratory animals after subchronic exposure to methidathion are summarized in Table 13. Clinical signs observed in oral and dermal subchronic toxicity studies of varying length included lethargy, anorexia, labored or rapid breathing, hunched posture, ataxia, tremors, soft feces, and low body temperature. Reductions in body weights and food consumption were also seen. Pathological findings included changes in hematological values

Table 13. Subacute/Subchronic Effects of Methidathion and Their Respective NOELs and LOELs

Species	Exposure	Effect	NOEL (mg/kg/day)	LOEL (mg/kg/day)	Ref.[a]
Oral					
Rat[b]	9 days, gavage	Maternal: Reduced body weights and food consumption	1.0	2.5	1
Rat[b]	9 days, gavage	Maternal: Death, cholinergic signs, reduced body weights and food consumption	1.0	7.5	2
Rat[b]	9 days, gavage	Maternal: Death, cholinergic signs, reduced body weights and food consumption	1.0	2.5	3*
Rabbit[b]	13 days, gavage	Maternal: Stool alterations, reduced body weights	-----	10.0	4
Rabbit[b]	13 days, gavage	Maternal: Cholinergic signs	6.0	12.0	5*
Mouse	28 days, diet	Reduced ChE[c] activity in RBCs (MF: 57%[d]) and brain (M: 49%; F: 65%)	4.2	18.0	6
Rat	4 weeks, diet	Reduced RBC ChE activity (M&F: 62%-77%)	0.25	0.83	7
Rat	4 weeks, diet	Unspecified cholinergic signs, fatty deposits in liver	2.5	5.0	7
Rat[e]	2-gen., 10 wks premating, diet	Parental: Reduced mating index (M), alopecia (F), poor maternal care, tremor (F) Fetal: Reduced pup weights and signs of maternal neglect	0.4 0.4	2.2 2.2	8*
Rat[f]	**90-days, diet**	**Reduced ChE activity in RBCs (M: 74-81%; F: 56-75%), cerebral cortex (M: 74%), striatum (F: 63%), and hippocampus (F: 76%)**	**0.2**	**0.6**	**9***
Rat	22 weeks, diet	Reduced ChE activity (70-75%, unclear if blood or brain)	0.2	0.8	7
Rat	6 months, diet	Reduced RBC ChE activity (% not reported)	0.2	1.1	7
Dermal					
Rat	3 hrs/day, 5 days/wk, 4 wks	None	12.0	-----	7
Rabbit	6 hrs/day, 22 days	None	20.0	-----	10
Rabbit	6 hrs/day, 21 days	Death, lesions in stomach and heart	-----	1.0	11

a References: 1. Fritz, 1976b; 2. Marcsinsin *et al.*, 1986; 3. Mainiero *et al.*, 1987; 4. Wallace, 1986; 5. Hummel, 1987; 6. Albanese, 1976; 7. Geigy, 1964; 8. Salamon, 1987; 9. Chow and Turnier, 1995; 10. Folinusz *et al.*, 1986; 11. Osherhoff, 1987b.
b Developmental toxicity study: Only maternal effects observed after the first few days were included.
c ChE = Cholinesterase
d Percent of control activity
e Reproductive toxicity study
f Neurotoxicity study
* Acceptable study based on FIFRA guidelines

suggesting anemia, changes in serum enzyme levels suggesting liver toxicity, reduced brain ChE activity, and lesions in the liver, gallbladder, stomach, kidney and heart. The lowest LOEL in a standard subchronic toxicity study was 1 mg/kg/day based on deaths and histological lesions in the stomach and heart in rabbits after a 21-day dermal exposure (Osherhoff, 1987). This study had one major deficiency in that there was an incomplete histopathological examination of the control and high-dose animals.

In addition to the standard subchronic toxicity studies, Table 13 includes several developmental toxicity studies where maternal effects were observed after subacute exposure for 1 to 2 weeks. Maternal signs observed after subacute exposure to methidathion included tremors, ataxia, salivation, lacrimation and other ocular discharge, exophthalmia, miosis, vaginal bleeding and unthriftiness. Reductions in food consumption and maternal body weights were also seen. The lowest maternal NOEL in an acceptable developmental toxicity study was 1 mg/kg/day based on death, lethargy, tremors, salivation, lacrimation, exophthalmia, raspy respiration, vaginal bleeding, chromodacryorrhea, and reduced food consumption and body weights (Mainiero *et al.*, 1987).

Any effects observed in reproductive toxicity studies were also included in Table 13. The effects observed in the parental generations of the reproductive toxicity studies for methidathion included tremors, alopecia, reductions in food consumption and body weights, reduced mating index and poor maternal care. The effects observed in pups included tremors, signs of maternal neglect (cool to touch, starving, weak or lethargic), reduced pup weights and reduced survival. In the one acceptable study, the parental NOEL of 5 ppm (0.4 mg/kg/day) was based on alopecia and tremors (females), reduced mating index, and poor maternal care (Salamon, 1987). The reproductive NOEL in this study was also 5 ppm (0.4 mg/kg/day) based on reduced pup weights and signs of maternal neglect.

One 90-day subchronic neurotoxicity study in rats was available for methidathion (Chow and Turnier, 1995). Females exhibited clinical signs (infrequent stools, transient tremors, chromorhinorrhea), changes in FOB parameters, and reductions in body weights at 100 ppm (7.19 mg/kg/day). The changes in FOB parameters included neuromuscular effects (abnormal gait, reduced forelimb and hindlimb grip strength), CNS signs (tremors, stereotypy, bizarre behavior) and sensorimotor effects (increased response to touch, sound and tail pinch). Significant reductions in ChE activity in the cerebral cortex, cerebellum, hippocampus and striatum were also seen in both sexes. The NOEL for this study was 3 ppm (M: 0.182 mg/kg/day; F: 0.198 mg/kg/day) based on the reduced ChE activity in RBCs (M: 74-81%; F: 56-75% of controls - wks 4-13) cerebral cortex (M: 74% of controls - wks 2-4), striatum (F: 63% of controls - wk 13) and hippocampus (F: 76% of controls - wk 13). There was some uncertainty about the toxicological significance of the ChE inhibition in the cerebral cortex of males since females had more pronounced ChE inhibition in this region at higher dose levels and males did not exhibit any clinical signs, changes in FOB parameters or changes in maze activity at any dose level. However, the cortex ChE activity in males at 10 ppm was consistently reduced to about 75% of control activity throughout the study (although it was not always statistically significant). Therefore, DPR toxicologists made the health protective assumption that the reduced ChE activity in the cerebral cortex of males at 10 ppm (0.6 mg/kg/day) was of toxicological significance.

Reduced RBC and brain ChE activity appear to be the most sensitive endpoints with subchronic exposure to methidathion. ChE activity was not measured in any of the developmental or reproductive toxicity studies, so the NOELs for these studies might have been lower if ChE activity had measured. There does not appear to be any significant seasonal variation in dietary or drinking water exposure to methidathion; however, the occupational and ambient air exposure to methidathion were seasonal. Therefore, the 90-day neurotoxicity study was selected as the definitive study for evaluating seasonal occupational and ambient air exposure to methidathion because it had the lowest subchronic NOEL and it met FIFRA guidelines. The critical NOEL was 0.2 mg/kg/day based on the reduced ChE activity in the RBCs of both sexes (56-81% of controls), in the cerebral cortex of male rats (74%) and in the striatum (63% of controls) and hippocampus (76% of controls) of female rats.

Chronic Toxicity

The effects observed in laboratory animals with chronic exposure to methidathion are summarized in Table 14. Effects seen in laboratory animals with chronic exposure to methidathion were similar to those seen with subchronic exposure, except hepatotoxicity was more common. In addition, ulceration and inflammation of the skin and focal accumulation of foamy macrophages in the alveoli were seen in a chronic feeding study with rats (Yau *et al.*, 1986). Hepatotoxicity and brain ChE inhibition were the most common effects seen. Mice appear to be significantly less sensitive to the hepatotoxicity and brain ChE inhibition since the NOELs in mice were nearly an order of magnitude higher than in rats and dogs. The lowest LOEL (0.2 mg/kg/day) was observed in a 2-year rat chronic toxicity study based on slightly reduced brain ChE activity (M: 86%; F: 92%) (Johnston, 1967). There were multiple deficiencies in this older rat study including a high mortality rate due to pulmonary infections, no analysis of test compound or feed to verify purity or concentration, insufficient hematological and clinical chemistry analysis, incomplete histopathology and incomplete individual data. The findings from this older study were superceded by those from a more recent study conducted by Yau *et al.* (1985) which met FIFRA guidelines and established a NOEL of 0.17 mg/kg/day based on clinical signs, reduced body weights, reduced food and water consumption, reduced ChE activity in RBCs (M: 78%; F: 82% of controls) and brain (M: 49%; F: 48% of controls), reduced liver weights, and skin lesions. A similar NOEL, 0.15 mg/kg/day, was seen in dogs based on elevated liver enzymes in the serum and histological lesions in the liver (Chang and Walberg, 1991). The rats appear to be slightly more sensitive to the neurotoxicity of methidathion whereas the dogs appear more sensitive to the hepatotoxicity. The different responses could be due to differences in metabolism (either in the rate or the major pathways) between dogs and rats. The dog study conducted by Chang and Walberg (1991) was selected as the definitive study for evaluating chronic exposure to methidathion since it had a slightly lower NOEL and it met FIFRA guidelines. The critical NOEL for chronic exposure was 0.15 mg/kg/day based on elevated liver enzymes in the serum and histological lesions in the liver.

Oncogenicity - Weight of Evidence

The genotoxicity data for methidathion was predominantly negative. The negative tests included 8 gene mutation studies (4 reverse-mutation assays with *Salmonella typhimurium*, 1 reverse-mutation assay with *Escherichia coli*, and 3 host-mediated assays), 2 chromosome aberration studies (an *in vivo* micronucleus assay in Chinese hamster and a dominant lethal assay

Table 14. Chronic Effects of Methidathion and Their Respective NOELs and LOELs

Species	Exposure	Effect	NOEL	LOEL	Ref.[a]
			(mg/kg/day)		
Mouse	18-19 months, diet	Histological lesions in the liver of males	1.5	15.0	1
Mouse	18-23 months, diet	Discolored urine, reduced RBC ChE activity (F: 64-74%[c]), elevated serum ALT levels, histological lesions in liver and gall bladder (M)	1.4	6.7	2*
Rat	2 years, diet	Reduced brain ChE activity (M: 86%; F: 92%)	-----	0.2	3
Rat	104 weeks, diet	Clinical signs, reduced body weights, food and water cons., reduced ChE activity in RBCs (M: 78%; F: 82%) and brain (M: 49%; F: 48%), reduced liver weights, skin lesions	0.17	1.77	4*
Dog	105 weeks, diet	Elevated liver enzymes in serum, histological lesions in liver and spleen	0.12	0.48	3
Dog	**1 year, diet**	**Elevated liver enzymes in serum, histological lesions in the liver**	**0.15**	**1.33**	**5***
Monkey	23 months, gavage	Reduced ChE activity in plasma (M&F: 39%) and RBCs (M&F: 60-76%)	0.25	1.0	6

a References: 1. IBT, 1980; 2. Goldenthal, 1986; 3. Johnston, 1967; 4. Yau *et al*., 1984; 5. Chang and Walberg, 1991; 6. Goldberg, 1971.
b ChE = cholinesterase
c Percent of control activity
* Acceptable study based on FIFRA guidelines

in mice) and 6 assays for DNA damage (5 unscheduled DNA synthesis assays and 1 rec assay) (Lippens et al., 1983; Arni, 1980a,b&c; Simmon and Poole, 1977; Satou et al., 1979; Strasser, 1980; Fritz, 1976a; Hool, 1980b; Hertner, 1988 & 1990; Ciba-Geigy, 1982; Tong 1982a&b). However, only the dominant lethal assay and 2 of the autoradiographic DNA repair tests met FIFRA guidelines (Fritz, 1976a; Hertner, 1988 & 1990). The most toxicologically relevant assays were the reverse mutation assays with *Salmonella typhimurium* (Ames tests) and the *in vivo* micronucleus assay in the Chinese hamster. The Ames tests are relatively sensitive tests for evaluating mutagenic potential. Although all the Ames test had deficiencies, the negative results are more meaningful since they were reproduced in several different laboratories over a range of doses with and without metabolic activation. The micronuclei is a useful test for evaluating the potential of chemicals to induce chromosomal anomalies. There is a high correlation between agents that induce chromosomal aberrations and micronuclei. The negative results from this assay are more meaningful because it was an *in vivo* assay in a mammalian species. The genotoxicity tests for several metabolites of methidathion were also negative including Ames tests for 3 metabolites and an *in vivo* micronucleus assay for one metabolite (Arni, 1980d-f; Hool, 1980c). On the other hand, there is weak evidence that methidathion is genotoxic. Positive responses were reported in a gene conversion/forward mutation assay with *Saccharomyces cerevisiae* and an *in vitro* sister chromatid exchange assay with Chinese hamster V79 cell line (Arni and Muller, 1981; Chen *et al.*, 1981). An equivocal response was seen in an *in vivo* sister chromatid exchange assay (Hool, 1980a). The gene conversion/ forward mutation assay is a good screen for mutagenic activity, but its usefulness is limited when extrapolating the results to higher organisms. The biological significance of a positive sister chromatid exchange assay is also unclear since it represents an exchange of identical information. While the vast majority of genotoxicity tests for methidathion suggests that it does not act directly on DNA, there is some uncertainty based on the few positive tests.

U.S. EPA performed a structure-activity relationship search for chemicals with structural similarity to methidathion (Quest *et al.*, 1990). Only two pesticides were identified as structurally similar, prothidathion and lythidathion. No toxicity data were available for these pesticides since they are not registered in the United States.

There is evidence that methidathion is oncogenic based on a significant increase in the incidence of hepatocellular adenomas and carcinomas in male mice in two different oncogenicity studies (IBT, 1980; Goldenthal, 1986). In one mouse study, an increase in hepatocellular adenomas and carcinomas was seen in males at 100 ppm (IBT, 1980). However, this study had numerous major deficiencies including no food consumption data, control group mistakenly dosed with treated feed in month 14, apparent degradation of the test material in the first 8 months, and no hematology data. In an acceptable mouse oncogenicity study, there was also a significant increase in the incidence of hepatocellular adenomas and carcinomas at 50 and 100 ppm (Goldenthal, 1986). The incidence of both tumor types exhibited a dose-related trend that was highly significant when analyzed separately or combined (Table 5). In addition, 3 animals at 100 ppm had multiple liver tumors. The increase in hepatocellular adenomas was significant by pairwise comparison to controls at all dose levels. However, the incidence in the controls was unusually low and only the incidence at 100 ppm was clearly outside the historical control range for this laboratory (0-27%) (Table 6) (Quest *et al.*, 1990). The increase in hepatocellular carcinomas was also significantly different than controls at 100 ppm. When combined, the increase in hepatocellular adenomas and carcinomas was significant at 50 and 100 ppm. The incidence of carcinomas and combined adenomas/carcinomas exceeded the historical control range (carcinomas: 0-10%; combined: 5-32%) at 50 and 100 ppm. The proportion of malignant tumors at 50 and 100 ppm (62 and 45%, respectively) was greater than historical controls (mean 34%), but not concurrent controls (89%).

There appeared to be a reduction in the time to tumor in males at 100 ppm since the proportion of tumor-bearing animals that died early was higher (76%) when compared to concurrent controls (33%). In fact, the shortest time to tumor (445 days) was seen in a male at 100 ppm. However, if the time to death of the liver tumor-bearing males that died early is compared, the means are similar (618 days for controls vs. 608 days at 100 ppm). If only the males where liver tumors were considered the cause of death were included, the mean time to death was actually higher at 100 ppm (645 days) than controls (618 days). The liver tumors were considered the cause of death for only 11 of 29 male mice (38%) at 100 ppm that died early with liver tumors compared to 3 of 3 male mice (100%) in the control group.

It is noteworthy that the significant increases in neoplastic liver lesions in male mice occurred at dose levels that also caused significant increases in non-neoplastic liver lesions (Table 4). There was no increase in neoplastic liver lesions in females despite a slight increase in non-neoplastic lesions at 100 ppm. However, the incidence of non-neoplastic liver lesions in females at 100 ppm (bile stasis 24%, chronic hepatitis 17%) was considerably lower than in males at 50 ppm (bile stasis 51%, chronic hepatitis 49%). There was also no significant increase in neoplastic or non-neoplastic liver lesions in either sex of rats up to the highest dose level, 100 ppm (~ 5 mg/kg/day). The apparent association of the hepatotoxicity with the liver tumors suggest that an increase in cell proliferation or turnover may be responsible for the increase in tumors. An argument could be made that the increase in mortalities (68% versus 42% in controls) and the high incidence of non-neoplastic lesions in the liver (bile stasis and chronic hepatitis - 98%) in male mice at 100 ppm indicate that this dose level was excessively toxic and the tumor response at this dose level should be disregarded in the evaluation of the oncogenic potency of methidathion. It is less clear if the severity of hepatotoxicity at 50 ppm was sufficient to disregard the increase in tumors at this dose level. Furthermore, there is inadequate mechanistic data to demonstrate that the excessive toxicity at the high dose was solely responsible for the increase in tumors.

Quantitative Assessment of Oncogenic Effects

There is little doubt that the increase in liver tumors in male mice is treatment-related. There was a clear dose-response relationship and an increase in these tumors was seen in male mice in two studies, although one study had major deficiencies (IBT, 1980; Goldenthal, 1986). Furthermore, in the study that met FIFRA guidelines, there was an increase in the multiplicity of tumors at the highest dose level, a possible increase in the proportion of malignant tumors, and a possible reduction in the time to tumor. On the other hand, the weight of evidence for oncogenicity was limited because it involved a common tumor type in only one tissue site in only one sex of one species. There was no evidence of oncogenicity in female mice or in two chronic rat studies for methidathion (IBT, 1980; Goldenthal, 1986; Johnston, 1967; Yau *et al.*, 1986). Moreover, the genotoxicity data for methidathion were predominantly negative. The only positive results were reported in two assays of questionable biological significance (a gene conversion/forward mutation assay with *Saccharomyces cerevisiae* and an *in vitro* sister chromatid exchange assay with Chinese hamster V79 cell line). In addition, there appears to be an association between the incidence of hepatotoxicity and liver tumors. The U.S. EPA has classified methidathion as a Group C carcinogen (i.e., possible human carcinogen), but did not consider the evidence sufficient to quantitate an oncogenic potency factor (Quest *et al.*, 1990). The FAO/WHO Joint Meeting on Pesticide Residues (JMPR) also did not consider the evidence sufficient to warrant calculating an oncogenic potency factor (Caris, 1992). Although DPR toxicologists agree that the weight of evidence is limited, the mode of action is uncertain. Direct

DNA interaction could not be eliminated based on the few positive genotoxicity tests. The association between the hepatotoxicity and the liver tumors suggests secondary DNA effects from a possible increase in cell proliferation; however, there was no mechanistic studies to support this possibility. The U.S. EPA Guidelines for Carcinogen Risk Assessment recommends that when the mode of action is not known that a linear approach be used as a default (U.S. EPA, 2005). Consequently, a linear approach was used to evaluate the oncogenic potential of methidathion.

The combined incidence of hepatocellular adenomas and carcinomas in male mice in the oncogenicity study conducted by Goldenthal (1986) was used to estimate oncogenic potency. Due to the reduced survival of male mice at the highest dose tested, 100 ppm, the multistage-Weibull time-to-tumor model, MULTI-WEIB, was used to estimate the oncogenicity potency. The dosages for male mice (0, 0.4, 1.4, 6.7 or 13.1 mg/kg/day) were first converted to human equivalent dosages (0, 0.06, 0.20, 0.97, 1.90 mg/kg/day) by multiplying by an interspecies scaling factor of body weight to the 3/4 power $[(BWt_A/BWt_H)^{0.25} = (0.030\text{ kg}/70\text{ kg})^{0.25} = 0.144]$ (U.S. EPA, 1992). The estimated oncogenic potency for methidathion ranged from 0.34 $(\text{mg/kg/day})^{-1}$ (maximum likelihood estimate or MLE) to 0.53 $(\text{mg/kg/day})^{-1}$ (95% upper bound or 95% UB).

B. EXPOSURE ASSESSMENT

Dietary Exposure

Introduction

DPR evaluates the risk of human exposure to an active ingredient in the diet using two processes: (1) use of residue levels detected in foods to evaluate the risk from total exposure, and (2) use of tolerance levels to evaluate the risk from exposure to individual commodities (see Section VI. Tolerance Assessment of this document). For evaluation of risk to detected residue levels, the total exposure in the diet is determined for all label-approved raw agricultural commodities (RACs), processed forms, and animal products (meat and milk) that have established U.S. EPA tolerances. Tolerances may be established for the parent compound and associated metabolites. DPR considers these metabolites and other degradation products that may be of toxicological concern in the dietary assessment.

Residue Data

The residue data for the dietary exposure assessments are based on DPR and federal monitoring programs, field trials, and survey studies. In absence of data, surrogate data from the same crop group, as defined by U.S. EPA, or U.S. EPA tolerances are used. Residue levels that exceed established tolerances are not utilized in the dietary exposure assessments. Over-tolerance incidents are investigated by DPR Pesticide Enforcement Branch and are relatively infrequent. The potential risk from consuming commodities with residues over tolerance levels is evaluated by the Medical Toxicology Branch using an expedited acute risk assessment process.

DPR has two major sampling programs: priority pesticide and marketplace surveillance. Samples from the priority pesticide program are collected from fields known to have been treated with the specific pesticides. For the marketplace surveillance program, samples are collected at the wholesale and retail outlets, and at the point of entry for imported foods. The sampling strategies for both priority pesticide and marketplace surveillance are similar and are weighted toward such factors as pattern of pesticide use; relative number and volume of pesticides typically used to produce a commodity; relative dietary importance of the commodity; past monitoring results; and extent of local pesticide use.

(DPR had two additional monitoring programs prior to 1991. The preharvest monitoring program routinely examined the levels of pesticides on RACs in the field at any time during the growth cycle. Commodities destined for processing were collected in the field no more than 3 days prior to harvest, at harvest, or post-harvest before processing.)

The U.S. Food and Drug Administration (FDA) has three programs for determining residues in food: (1) regulatory monitoring, (2) total diet study, and (3) incidence/level monitoring. For regulatory monitoring, surveillance samples are collected from individual lots of domestic and imported foods at the source of production or at the wholesale level. In contrast to the regulatory monitoring program, the total diet study monitors residue levels in the form that a commodity is commonly eaten or found in prepared meals. The incidence/level monitoring program is designed to address specific concerns about pesticide residues in particular foods.

The U.S. Department of Agriculture (USDA) is responsible for the Pesticide Data Program (PDP), a nationwide cooperative monitoring program. The PDP is designed to collect objective, comprehensive pesticide residue data for risk assessments. Several states, including California, collect samples at produce markets and chain store distribution centers close to the consumer level. The pesticide and produce combinations are selected based on the toxicity of the pesticide as well as the need for residue data to determine exposure. In addition, USDA is responsible for the National Residue Program that provides data for potential pesticide residues in meat and poultry. These residues in farm animals can occur from direct application, or consumption of commodities or by-products in their feed.

Primary Residues

Most of the residue values for RACs came from DPR's monitoring programs from 1992 to 1995 (DPR, 1993b, 1995b, 1996c & 1997b). DPR's multi-residue screen can detect both methidathion and its oxygen analog. The high and mean residue levels found during this period are summarized in Table 15. For the acute dietary assessment, the assumption was made that all commodities are consumed at the high residue value. The high value was either the highest measured residue level at or below the tolerance for methidathion on a commodity (CFR, 1998) or the 95th percentile, if there were more than 300 samples for a commodity. For methidathion, the tolerances are for the parent compound only on agricultural crops and for the oxygen analog, sulfoxide and sulfone metabolites in animal products. For the chronic dietary assessment, the assumption was made that all commodities are consumed at the mean or average residue level everyday on an annual basis. The DPR monitoring data do not account for potential change in residue levels due to (1) washing and peeling, and (2) food preparation and processing (e.g., cooking and canning).

Table 15. Methidathion Residues in Raw Agricultural Commodities from DPR's Monitoring Programs from 1992 to 1995[a]

Raw Agricultural Commodity	No. of Samples	High Value[b] (ppm)	Mean Value[c] (ppm)
Apple	815	0.010	0.005
Apricot	143	0.010	0.005
Artichoke	170	0.040	0.005
Cherry	110	0.010	0.005
Grapefruit	339	0.128*	0.011
Kiwi fruit	194	0.010	0.005
Kumquat	9	0.010	0.005
Lemon	385	0.057*	0.007
Lime	338	0.026*	0.006
Nectarine	299	0.010	0.005
Orange	934	0.564*	0.152
Peach	362	0.010	0.005
Pear	593	0.010	0.005
Plum	385	0.010	0.005
Quince	19	0.010	0.005
Tangelo	31	0.010	0.005
Tangerine	257	1.030	0.015

a Residues from DPR's monitoring sampling programs 1 (priority pesticide) and 4 (marketplace surveillance).
b The high value represents the highest residue level detected in any sample, except when there were more than 300 samples. In these cases (which are indicated by *), the high value is the 95th percentile of all the residues, assuming the limit of quantitation (LOQ = 0.01 ppm) for the samples with no detectable residues.
c When no residue was detected, ½ of the LOQ was used in calculating the mean for a commodity.

If there were no residues detected, then the high and mean residue levels were set at the limit of quantitation (LOQ) and ½ of the LOQ, respectively. The methidathion LOQ was 0.01 ppm for DPR monitoring programs. For a few commodities that had no monitoring data, residues from a surrogate crop were used instead. Residues from apples were substituted for crabapples and residues on orange peel were substituted for citrus citron. For several other commodities with no monitoring data or good surrogates, the residue levels were assumed to be at the tolerance level for acute exposure and ½ of the tolerance level for chronic exposure (CFR, 1999). This included nuts (tolerance = 0.05 ppm), olives, (0.05 ppm), mangoes (0.05 ppm), kiwi fruit (0.1 ppm), sugar apples (0.2 ppm), carambola (0.1 ppm), longan fruit (0.1 ppm), sorghum (0.2 ppm), sunflower seeds (0.5 ppm), safflower seeds (0.5 ppm) and cottonseed (0.2 ppm). Although there was a tolerance for potatoes, this commodity was not included in the dietary exposure assessment for methidathion since there are no registered uses. U.S. EPA has proposed revoking the tolerance for potatoes for this reason during the reregistration process (U.S. EPA. 1998).

Generally, residue data were not available for processed commodities. Since no residue data were available, the residues in the processed commodities were estimated from the fresh commodity by multiplying by the default adjustment factors that account for the loss of water. Since other physical properties of methidathion could affect whether it concentrates in processed foods, these residue levels are only theoretical. Nonetheless, if the residues in processed commodities were higher than the tolerance for the RAC, they would be considered illegal since no food additive tolerances were established for these commodities. Residue data for processed oranges were available which indicated that the residues decreased in peeled fruit and juice rather than increased (Burnett, 1992). Based on these studies, the adjustment factors for citrus juice and peeled citrus fruit meal were reduced to 0.1. The default adjustment factors for citrus juice were fairly similar (1.8 to 2.3); however, the default adjustment factors for concentrated citrus juice varied more (6.0 to 11.4), presumably due to different water content. Therefore, the new adjustment factors for the citrus juice concentrates were estimated by multiplying the new adjustment value for citrus juice, 0.1, by the ratio of the old default value for the concentrate to the old default value for the juice. The resulting new adjustment factors were 0.39, 0.57, 0.30, and 0.32 for orange, grapefruit, lemon, lime and tangerine juice concentrate, respectively. The residue data on processed oranges indicated that the residue levels were higher in orange peel than the whole fruit. Therefore, the adjustment factor for citrus peel was changed to 2.5.

Since dietary exposure assessments can be very labor intensive, DPR toxicologists use a tiered approach with additional refinements when the risk for adverse health effects in humans is considered too high based on the criteria described in the risk appraisal section. Some of the more common refinements to the exposure estimate are: 1) use of residue monitoring data where commodities are analyzed closer to the point of consumption, 2) use of residue monitoring data with a lower detection limit (which is important when no residues are detected), 3) adjusting for the percent of a crop that is treated with a pesticide, and 4) elimination of residues on commodities for which U.S. EPA has proposed canceling the tolerance. The initial dietary analysis for methidathion using DPR monitoring data and tolerances was considered as Tier 1. Since the estimated chronic dietary exposure appeared too high based on an estimated oncogenic risk greater than 10^{-6}, the chronic dietary exposure was further refined. In a critical commodity analysis (TAS, 1996a), several commodities were identified as contributing significantly to the overall anticipated dietary exposure to methidathion based on the DPR monitoring data. In the Tier 2 analysis, the residue values for several of these high consumption commodities was refined by using USDA's PDP data which analyzed commodities closer to the point of consumption (USDA, 1996b, 1997, 1998a&b). In the PDP monitoring program, commodities are usually washed and peeled if normally consumed that way. In addition, the LOQs for the PDP monitoring program were often lower, especially for California samples (0.003 ppm), than for DPR's market basket monitoring program (0.01 ppm). The commodities for which PDP data were used are shown in Table 16 and include oranges (whole and juice), apples (whole and juice), peaches and pears. Samples were from one to three years, depending on how many samples were available. When sufficient data was available, PDP data from California was used exclusively since they had a lower LOQ. This applied to apple juice and whole peach residue values.

Since the estimated oncogenic risk was still greater than 10^{-6} after including the PDP data, a Tier 3 analysis was done for chronic dietary exposure. The current DPR default assumption for acute and chronic dietary exposure analysis is that 100% of any crop is treated

Table 16. Methidathion Residues in Raw Agricultural Commodities from USDA's PDP Monitoring Programs

Raw Agricultural Commodity	N	High Value[a]	Mean Value[b]	Source & Years
		(ppm)	(ppm)	
Apple, whole	327	0.01	0.005	National - 1995 & 1996
Apple, juice	860	0.003	0.0015	California only- 1996 & 1997
Orange, whole	1282	0.0068*	0.00182	National - 1995 & 1996
Orange, juice	692	0.005	0.00155	National - 1997
Peach	355	0.003	0.0015	California only - 1995 & 1996
Pear	708	0.01	0.005	National - 1997

a The high value represents the highest residue level detected in any sample, except when there were more than 300 samples. In these cases (which are indicated by *), the high value is the 95th percentile of all the residues, assuming the limit of quantitation (LOQ = 0.003-0.014 ppm) for the samples with no detectable residues. The LOQ for California monitoring (0.003 ppm) was using lower than for the rest of the country (~0.01 ppm)
b When no residue was detected, ½ of the LOQ was used in calculating the mean for a commodity.

with the pesticide under consideration. However, when reliable data are available that indicate that less than 100% of a commodity is treated with a specific pesticide, then the chronic dietary residue values can be adjusted to take percent crop treated (PCT) into consideration. In the Tier 3 analysis for methidathion, estimates of the PCT were based on the DPR Pesticide Use Report (DPR, 1995c,1996d & 1996e), California Department of Food and Agriculture (CDFA) crop statistic (CDFA, 1994) and USDA agricultural statistics (USDA, 1992, 1994a&b, 1996a). While the pattern of pesticide use is expected to fluctuate from year to year, the PCT was determined from data collected over several years. The highest PCT values, rounded to the nearest 5%, was used in the chronic exposure analysis. PCT data were not available for all commodities. The commodities adjusted for PCT included apples (15%), oranges (20%), peaches (35%), pears (10%), almonds (15%), walnuts (10%), olives (10%), kiwi fruit (15%), and cotton (1%). The PCT was taken into consideration when the average residue values were calculated for chronic exposure. For samples with nondetectable residues, zero was assumed for the proportion of the samples corresponding to the percent not treated instead of ½ of the LOQ. Consequently, the average residue for some commodities could be less than ½ of the LOQ.

Secondary Residues

No residue monitoring data were available for animal products. Although U.S. EPA has proposed revoking tolerances for methidathion in all animal products, these residues were included in this dietary exposure assessment since the tolerances have not been officially revoked (U.S. EPA, 2000b). The anticipated residues in meat, milk, poultry and eggs were estimated by first estimating the amount of residues in animal feed. Table 17 summarizes the anticipated methidathion residues in feed for cattle, pork and poultry based on estimated maximum percent of livestock feed in Table II of U.S. EPA's Pesticide Assessment Guidelines, Subdivision O, Residue Chemistry (U.S. EPA, 1994). The maximum anticipated residues in cattle, swine, and poultry feed were 0.318, 0.151, and 0.030 ppm, respectively. The mean

Table 17. Anticipated Methidathion Residues in Feed for Cattle, Swine and Poultry

Raw Agricultural Commodity	Dry Matter (%)	Diet (%)	Maximum Residue (ppm)	Max. Feed Contribution (ppm)	Mean Residue (ppm)	Mean Feed Contribution (ppm)
Cattle						
Almond hulls[a]	90	25	0.660	0.183	0.191	0.053
Citrus pulp, wet[b]	21	40	0.056	0.107	0.015	0.029
Cottonseed, meal[c]	89	10	0.024	0.003	0.009	0.001
Safflower, meal[d]	91	25	0.090	0.025	0.035	0.010
Total Contribution				0.318		0.093
Pork						
Almond hulls	90	10	0.660	0.073	0.191	0.021
Apple pomace, wet[e]	40	25	0.010	0.006	0.005	0.003
Citrus pulp, wet	21	15	0.056	0.040	0.015	0.011
Cottonseed, meal	89	25	0.024	0.007	0.009	0.003
Safflower, meal	91	25	0.090	0.025	0.035	0.010
Total Contribution				0.151		0.048
Poultry						
Cottonseed, meal	89	20	0.024	0.005	0.009	0.002
Safflower, meal	91	25	0.09	0.025	0.035	0.010
Total Contribution				0.030		0.012

a Residue estimated from a field trial study on almond hulls (Mattson, 1975)
b Residue estimated from DPR residue monitoring data for whole oranges from 1992-1995 and assuming residues in pulp are one tenth that in whole fruit based on an residue study on processed orange commodities (Burnett, 1992).
c Residue estimated from a field trial study on whole cottonseed (Ciba-Geigy, 1976) and assuming residues in meal are 0.12 times the amount in whole cottonseed based on a residue study on processed cottonseed commodities (Kahrs and Kanuk, 1969).
d Residue estimated from field trail studies on whole safflower seed (Ciba-Geigy, 1975; Ciba-Geigy, 1977)
e Residue estimated from DPR residue monitoring data for whole apples from 1992-1995.

anticipated residues in cattle, swine, and poultry feed were 0.093, 0.048, and 0.012 ppm, respectively.

The anticipated methidathion residues in cattle, swine and poultry tissues are summarized in Table 18. Tissue residues in cattle and swine were based on a metabolism study in which methidathion was administered in capsules to goats at 60 mg/day (equivalent to 47.5 ppm in feed) for four consecutive days (Emarani, 1992). Tissue residues in poultry were based on a metabolism study in which methidathion was administered to laying hens at 4 mg/day (equivalent to feed residue level of 40 ppm) for 7 days (Kennedy, 1992). The tissue residue levels in these metabolism studies were considered the sum of methidathion, its oxygen analog, sulfoxide and sulfone. The tissue residues were then adjusted by a distribution factor assuming that the residue in the tissue was proportional to the residue in the feed (i.e., the residues in the goat and hen tissues were divided by 47.5 ppm and 40 ppm, respectively). The distribution factor for each tissue was then multiplied by the anticipated maximum (acute) and mean (chronic) residues in cattle, swine and poultry feed in Table 18 to obtain the anticipated maximum and mean residues in meat, milk, poultry and eggs. Since U.S. EPA's Subdivision O does not include values for sheep, goats or horses, the anticipated residues for cattle tissues were used for them.

As mentioned earlier, U.S. EPA has proposed revoking all the tolerances for methidathion in animal products (U.S. EPA, 2000b). Since these tolerances have not been officially revoked, they were included in this dietary exposure assessment for methidathion. However, because the estimated oncogenic risk from dietary exposure to methidathion was slightly higher than 10^{-6} after PCT was taken into consideration, a Tier 4 analysis was performed with all of the secondary residues removed.

Consumption Database

The USDA directs the Nationwide Food Consumption Survey (NFCS) and the Continuing Survey of Food Intakes by Individuals (CSFII) (USDA, 1989-91). The NFCS is a geographically stratified probability sampling of U.S. households and is conducted every 10 years (1977-78 and 1987-88). The CSFII is an annual survey which reflects the current consumption pattern and has a greater focus on consumption data for vulnerable population subgroups (e.g., infants and children).

Acute Dietary Exposure

The acute dietary exposure analysis was conducted using the Exposure-4™ software program developed by Technical Assessment Systems, Inc (TAS) (see Appendix B for printout). The Exposure-4™ software program estimates the distribution of user-day (consumer-day) exposure for the U.S. population and specific subgroups (TAS, 1996a). A user-day is any day in which at least one food form from the label-approved commodities is consumed. Based on the 95th percentile of user-day exposure for all specific population subgroups in the Tier 1 analysis, the potential acute dietary ingestion of methidathion from all labeled uses ranged from 253 to 1,068 ng/kg/day (Table 19). Nursing infants less than one year old had the highest potential acute dietary exposure.

Table 18. Distribution Factors and Anticipated Tissue Residues in Cattle, Swine and Poultry

Tissue	Distribution Factor[a] (%)	Anticipated Methidathion Residue	
		Maximum[b] (ppb)	Mean[c] (ppb)
Cattle			
Muscle	0.29	0.92	0.27
Fat	0.03	0.10	0.03
Liver	0.29	0.92	0.27
Kidney	0.19	0.60	0.18
Milk	0.11	0.35	0.10
Swine			
Muscle	0.29	0.44	0.14
Fat	0.03	0.05	0.01
Liver	0.29	0.44	0.14
Kidney	0.19	0.29	0.09
Poultry			
Muscle	0.37	0.11	0.04
Fat	0.23	0.07	0.03
Liver	0.71	0.21	0.09
Eggs	0.44	0.13	0.05

a The distribution factors for cattle and swine were based on a metabolism study in which goats were administered methidathion in capsules at 60 mg/day (equivalent to 47.5 ppm in the feed) for 4 days (Emrani, 1992). The distribution factors for poultry were based on metabolism study in which laying hens were administered methidathion in capsules at 4 mg/day (equivalent to 40 ppm in the feed) for 7 days (Kennedy, 1992). The distribution factor is the ratio of the residue level in the tissue to the residue level in the feed.

b The maximum anticipated residues in tissues were derived by multiplying the distribution factor for the tissue by the maximum anticipated residue level in feed (e.g., the maximum residue in cattle muscle is 0.29% x 0.318 ppm = 0.77 ppb). The maximum anticipated residue levels in cattle, swine, and poultry feed were 0.318, 0.151, and 0.030 ppm, respectively.

c The calculation for the mean anticipated residues in tissues is identical to that for the maximum anticipated residues, except that the mean anticipated residue level in feed was used. The mean anticipated residue levels in cattle, swine and poultry feed were 0.093, 0.048, and 0.012, respectively.

Table 19. Potential Acute and Chronic Dietary Exposures to Primary and Secondary Methidathion Residues

Population Subgroup	Exposure Dosage (ng/kg/day)				
	Acute[a]	Chronic[b]			
	Tier 1	Tier 1	Tier 2	Tier 3	Tier 4
U.S. Population	418	34	15	5	3
Western Region	463	37	16	5	3
Nursing Infants (< 1 yr)	1,068	45	17	4	2
Non-nursing Infants (< 1 yr)	850	80	35	18	10
Children (1-6 yrs)	1,048	98	39	12	6
Children (7-12 yrs)	564	56	26	8	5
Females (13+ yrs/P/NN)	356	32	13	5	3
Females (13+ yrs/N)	496	43	19	7	5
Females (13-19 yrs/NP/NN)	358	28	12	3	2
Females (20+ yrs/NP/NN)	276	23	10	3	2
Males (13-19 yrs)	374	32	15	4	2
Males (20+ yrs)	253	21	11	3	2
Seniors (55+ yrs)	262	23	10	3	2
Workers (16+ yrs)	272	NA	NA	NA	NA

a Based on 95th exposure percentile for each user-day population subgroups.
b Based on the annual average daily dosage for each population subgroups.
P Pregnant
NN Not Nursing
N Nursing
NP Not pregnant
NA Not available. The TAS Exposure-1™ program does not calculate an exposure estimate for customized population subgroups, such as, workers 16 years and older.

Chronic Dietary Exposure

The potential chronic dietary exposure was calculated using the Exposure-1™ software developed by TAS (TAS, 1996b) (See Appendix B for printout). The program estimates the annual average exposure for all members of a designated population subgroup. Based on the Tier 4 analysis, the mean potential chronic dietary exposure for all population subgroups ranged from 2 to 10 ng/kg/day (Table 19). The population subgroup with the highest potential exposure was non-nursing infants less than 1 year old.

Drinking Water Exposure

Drinking Water Residues

Although methidathion has not been detected in any wells monitored by DPR from 1989 to 1996 (DPR, 1992, 1993a, 1994, 1995a, & 1997a), it has been detected by DPR and the U.S. Geological Survey in surface water monitored in California between 1991 and 1998 (Ross, 1992,1993; MacCoy *et al.*, 1995; Ross *et al.*, 1996; Bennet, 1997; Ganapathy *et al.*, 1997; Nordmark, 1997 &1998; Poletika and Robb, 1998; Ganapathy, 1999; Ross *et al.*, 1999; U.S. Geological Survey, in preparation). It is uncertain if any of the surface water monitored was used for drinking water, except for the Sacramento River near downtown Sacramento. It is also uncertain if the residues would persist after water treatment. However, the assumption was made that all the surface water monitored was used for drinking water and that the residue levels were unaffected by water treatment. For acute exposure, the 95th percentile of the residue level in surface water (0.654 ppb) was assumed for all water sources (tap, bottled, commercial processing, and other non-food based water). The 95th percentile was calculated assuming the residue in the samples with no detectable residue was equal to the LOQ. For chronic exposure, the mean of the residue level (0.029 ppb) was used for all water sources where ½ of the LOQ was used for non-detectable samples.

Drinking Water Exposure

The acute and chronic drinking water exposure analyses were also conducted using the Exposure-4™ and Exposure-1™ software programs (TAS, 1996a&b) (see Appendix B for printout). The water consumption data from the 1989-1991 USDA CSFII was used for both acute and chronic drinking water exposure analyses (USDA, 1989-91). Based on the 95th percentile of user-day exposure for all specific population subgroups, the potential acute exposure to methidathion in drinking water ranged from 29 to 181 ng/kg/day (Table 20). Non-nursing infants less than one year old had the highest potential acute drinking water exposure. The mean potential chronic drinking water exposure for all population subgroups ranged from 1 to 4 ng/kg/day (Table 20). The population subgroup with the highest potential exposure was also non-nursing infants less than 1 year old.

Combined Dietary and Drinking Water Exposure

The combined exposure to methidathion in food and water were analyzed using the Exposure-4™ and Exposure-1™ software programs (TAS, 1996a&b). The residues from the Tier 1 and 4 analyses were used for acute and chronic dietary exposure, respectively. The combined drinking water and dietary exposure is summarized in Table 20. The combined acute exposure to methidathion in drinking water and food is not equal to the sum of the acute dietary and drinking water exposures because each of these estimates is based on a distribution among consumers which changes as commodities or water are added or removed. Based on the 95th percentile of user-day exposure for all specific population subgroups, the potential combined acute exposure to methidathion from drinking water and diet (Tier 1) ranged from 273 to 1,067 ng/kg/day. Children 1 to 6 years old had the highest potential combined acute exposure. The potential combined chronic exposure to methidathion from drinking water and diet (Tier 4) for

Table 20. Potential Acute and Chronic Drinking Water Exposure to Methidathion

Population Subgroup	Exposure Dosage (ng/kg/day)			
	Acute[a]		Chronic[b]	
	Water	Water + Diet[c]	Water	Water + Diet[d]
U.S. Population	42	441	1	4
Western Region	46	483	1	4
Nursing Infants (< 1 yr)	63	878	1	3
Non-nursing Infants (< 1 yr)	181	916	4	14
Children (1-6 yrs)	62	1,067	1	7
Children (7-12 yrs)	42	579	1	5
Females (13+ yrs/P/NN)	33	371	1	4
Females (13+ yrs/N)	37	531	1	6
Females (13-19 yrs/NP/NN)	29	373	1	2
Females (20+ yrs/NP/NN)	34	296	1	3
Males (13-19 yrs)	33	391	1	3
Males (20+ yrs)	33	273	1	3
Seniors (55+ yrs)	31	280	1	3
Workers (16+ yrs)	34	293	NA	NA

a Based on 95th exposure percentile for each user-day population subgroups.
b Based on the annual average daily dosage for each population subgroups.
c Acute dietary exposure based on Tier 1 analysis.
d Chronic dietary exposure based on Tier 4 analysis.
P Pregnant
NN Not Nursing
N Nursing
NP Not pregnant
NA Not available. The TAS Exposure-1™ program does not calculate an exposure estimate for customized population subgroups, such as, workers 16 years and older.

all population subgroups ranged from 2 to 14 ng/kg/day. The population subgroup with the highest potential combined chronic exposure was non-nursing infants less than 1 year old.

Occupational Exposure

There are no residential, industrial or institutional uses of methidathion. A number of studies were available in which agricultural worker exposure to methidathion was evaluated; however, none of these studies were acceptable for reasons explained in the Exposure

Assessment Document (EAD) for methidathion (Beauvais, 2004). Therefore, exposure estimates for handlers were derived using the Pesticide Handler Exposure Database (PHED) developed by U.S. EPA, Health Canada and the American Crop Protection Association. PHED provides mean exposure estimates, but does not provide sufficient information to allow calculation of an upper bound estimate. A method for approximating the upper bound from PHED data was developed by the Worker Health and Safety Branch which multiplied the mean by constants that increased as the number of observations decreased (Powell, 2002). The 95th percentile is used for acute exposure to estimate the highest exposure an individual may realistically experience while performing label-approved activities. When the acute exposure estimate is based on surrogate data (i.e., PHED), the 90% upper confidence limit on the 95th percentile is used to account for some added uncertainty with using surrogate data. The acute exposure estimate is referred to as the Absorbed Daily Dosage (ADD). Default assumptions of 50% dermal absorption, 100% inhalation absorption and 70 kg body weight were used in the calculation of the ADD. The default dermal absorption value is based on a review of dermal absorption of several chemicals (Donahue, 1996). The default inhalation absorption was used in the absence of any chemical specific data. The ADDs for handlers ranged from 0.0034 mg/kg/day for mixer/loader/-applicators (M/L/As) using low-pressure handwands to 5.85 mg/kg/day for airblast applicators (Table 21).

For seasonal and chronic exposure estimates, the 90% upper confidence limit on the arithmetic mean estimate was used to account for the uncertainty due to using surrogate data. The seasonal exposure estimate is referred to as the Seasonal Absorbed Daily Dosage (SADD). The SADD represents the mean daily exposure during the high-use season. The estimated high-use season was 1, 1 and 3 months for aerial, airblast and groundboom activities, respectively. No seasonal or annual exposures were anticipated for backpack sprayer and low-pressure handwand activities. The SADDs for handlers ranged from 0.044 mg/kg/day for groundboom applicators to 1.55 mg/kg/day for aerial applicators (Table 21). The chronic exposure estimate or Average Absorbed Daily Dosage (AADD) is the SADD multiplied by the annual use months per year divided by the number of months per year. The estimated annual use months for handlers was 1, 2 and 2 months with aerial, airblast and groundboom activites, respectively. The AADDs for handlers ranged from 0.007 mg/kg/day for groundboom applicators to 0.243 mg/kg/day for airblast applicators. The Lifetime Average Daily Dosage (LADD) was calculated to estimate oncogenic risk for workers. The LADD is calculated by multiplying the AADD by 40 years of work in a lifetime and dividing it by 75 years in a lifetime. The LADDs for handlers ranged from 0.004 mg/kg/day for groundboom applicators to 0.130 mg/kg/day for airblast applicators.

The ADDs for field workers were calculated from dislodgeable foliar residues (DFRs) and transfer factors (TFs) using Equation 3 described in the EAD for methidathion (Beauvais, 2004). The default assumptions of 50% dermal absorption, an 8 hr workday and a 70 kg body weight were used in this equation. The ADDs were calculated using DFRs that corresponded to the expiration of the REIs (REI = 48 hrs, except for harvesting and thinning of citrus which was 30 days). The ADDs ranged from 0.0026 mg/kg/day for harvesting/thinning of citrus to 0.119 mg/kg/day for scouting in cotton and safflower fields (Table 21). The DFRs used in calculating the SADDs corresponded to the REI plus 3 days for most activities (i.e., DFRs for 5 days), except for thinning and harvesting of citrus in which the DFRs corresponded to the REI plus 10

Table 21. Estimated Exposure Dosages for Methidathion in Agricultural Workers[a]

Exposure Scenarios	Acute ADD[b] mg/kg/day	SADD[c] mg/kg/day	AADD[d] mg/kg/day	LADD[e] mg/kg/day
Handlers[f]				
Aerial				
M/L[g]	1.15	0.459	0.038	0.020
Applicator	4.65	1.55	0.129	0.069
Flagger	1.90	0.476	0.040	0.021
Airblast				
M/L	0.132	0.052	0.009	0.005
Applicator	5.85	1.46	0.243	0.130
Groundboom				
M/L	0.158	0.063	0.010	0.006
Applicator	0.176	0.044	0.007	0.004
Backpack sprayer				
M/L/A[h]	0.190	NA	NA	NA
Low-pressure handwand				
M/L/A	0.0034	NA	NA	NA
Field Workers[i]				
Scouting in cotton/safflower	0.119	0.0214	0.0053	0.0028
Harvesting/thinning citrus	0.0026	0.0014	0.0006	0.0003
Thinning artichokes	0.018	0.0032	0.0008	0.0004

a Exposure estimates from the Exposure Assessment Document (EAD) for methidathion by Beauvais (2004).

b ADD = Acute Absorbed Daily Dosage. Acute ADD = [(short-term exposure) x (acres/day) x (rate lb AI/acre)] / (70 kg body weight). The short-term exposure estimates are from Table 21 of the EAD for methidathion . The short-term exposure estimate is derived from PHED data using the 90% upper confidence limit on the 95[th] percentile. Acres treated per day assumptions differed for each application method. The acres applied per day were 350, 40 and 80 for aerial, airblast and groundboom scenarios, respectively. The application rates were 5, 5 and 3 lbs/acre for aerial, airblast and groundboom scenarios, respectively. The application rate and acres applied are not applicable to backpack sprayer and low-pressure handwand scenarios.

c SADD = Seasonal Absorbed Daily Dosage which is the 90% upper confidence limit on the mean estimate of the total absorbed dosage from PHED during high-end use season.

d AADD = Annual Average Daily Dosage which is the SADD x (annual use months per year) / 12 months.

e LADD = Lifetime Average Daily Dosage which is the AADD x (40 years of work in a lifetime) / (75 years in a lifetime).

f Handler exposure estimated from Pesticide Handlers Exposure Database (PHED, 1995). The estimated high-end use season was 1, 1, and 3 mnths for aerial, airblast, and groundboom activities, respectively. The estimated annual use is 1, 2, and 2 months for aerial, airblast, and groundboom activities, respectively. Seasonal and annual exposures were not anticipated for backpack sprayer and low-pressure handwand activities.

g M/L = Mixer/Loader

h M/L/A = Mixer/Loader/Applicator

i Field worker exposure was calculated from dislodgeable foliar residues (DFR) and transfer factors (TF) that are described in the EAD for methidathion (Beauvais, 2004). The seasonal and annual exposure were assumed to be the same for field workers with 3, 5 and 3 months for scouting in cotton/safflower, harvesting/thinning citrus, and thinning artichokes, respectively.

days (i.e, DFRs for 40 days). The SADDs for field workers ranged from 0.0014 mg/kg/day for harvesting and thinning of citrus to 0.0214 mg/kg/day for scouting in cotton and safflower fields. The AADDs for field workers were calculated as they were for handlers by amortizing the SADDs over a year (i.e., multiplying the SADD by the annual use months per year and dividing by 12 months). The annual use months for field workers was assumed to be 3, 5 and 3 months for scouting in cotton/safflower, harvesting/thinning citrus, and thinning artichokes, respectively. The AADDs for field workers were between 0.0006 and 0.0053 mg/kg/day. The LADDs for field workers ranged from 0.0003 to 0.0028 mg/kg/day.

Ambient and Application Site Exposure

Application Site Exposure

Individuals might be exposed to methidathion if they are working or standing adjacent to fields that are being treated or have recently been treated (i.e., bystander exposure). Acute exposure to methidathion in application site air was estimated from air monitoring conducted by the Air Resources Board (ARB) following an application to an orange grove in Tulare County in July 1991 (Beauvais, 2004). The highest residues were found in the north station where the time-weighted average (TWA) concentration was 0.80 $\mu g/m^3$. The ADDs for acute application site exposure were calculated using the 95% tolerance limits estimated with lognormal methods. A default value of 100% was used for inhalation absorption. The acute ADDs for bystanders were 519 ng/kg/day for children and 264 ng/kg/day for adults (Table 22). Seasonal and annual exposure to application site air is not expected because airborne concentrations are anticipated to reach ambient levels within a few days after the application.

Table 22. Estimated Exposure for the General Public to Methidation in Application Site and Ambient Air

Exposure Dosages	Children	Adults
Application Site[a]		
ADD[b] (ng/kg)	519	264
Ambient[c]		
ADD (ng/kg)	389	185
SADD[d] (ng/kg/day)	47	22
AADD[e] (ng/kg/day)	35	17

a Application site exposure dosages based on air concentrations in study by ARB (1991) in Tulare County.

b ADD = Absorbed Daily Dosage using the 95th percentile of the air concentrations. A default inhalation absorption of 100% was used. For more explanation of the calculations, see the exposure assessment document for methidathion prepared by Beauvais (2004).

c Ambient exposure dosages based on air concentrations at the Jefferson site in a study in Tulare County conducted by ARB.

d SADD = Seasonal Average Daily Dosage using on the mean air concentration at the Jefferson site during the monitoring period.

e AADD = Annual Average Daily Dosage = SADD x annual use months/12 months. Annual use months assumed to be 9 months per year.

Ambient Air Exposure

Ambient air monitoring data was also collected by ARB in Tulare County at four sites all within 0.25 mile of citrus groves (Sunnyside Union Elementary School in Strathmore, Jefferson Elementary School in Lindsay, Exeter Union High School in Exeter and the University of California Lindcove Field Station in Exeter) (Beauvais, 2004). The background site was the

ARB Ambient Air Monitoring Station in Visalia. Samples were collected during a 4-week interval between June 27 and July 25 of 1991. In 1991, Tulare County had the highest use of methidathion in California (75,582 lbs.) which occurred primarily in June and July. The Jefferson Elementary School in Lindsay was the only site with one or more samples above the limit of quantitation (LOQ = 0.3 µg/sample). Therefore, the risk estimates were initially calculated using the exposure estimates from this site, assuming that if they were acceptable at this location, they would be acceptable at the other three locations in Tulare County where the air concentrations were lower. The acute ADDs for the Jefferson site were 389 and 185 ng/kg/day for children and adults, respectively, using the 95th tolerance limits percentile and the default inhalation absorption of 100%. The SADDs were estimated to be 47 and 22 ng/kg/day for children and adults, respectively, using the mean ambient air concentration at the Jefferson site during the 4-week monitoring period. The AADD is the average air concentration for a year assuming the season of potential exposure is 9 months per year for methidathion. The AADDs for the Jefferson site were 35 and 17 ng/kg/day for children and adults, respectively.

Aggregate Exposure

Agricultural Workers

The exposure to methidathion through the diet, drinking water and residential (ambient) air was also considered in the potential exposure for agricultural workers (Table 23). The acute dietary and drinking water exposure to methidathion for workers (males and females 16 years and older) was estimated to be 0.293 µg/kg/day based on the 95th percentile of user-day exposure. The chronic dietary and drinking water exposure for workers was estimated to be 0.004 µg/kg/day based on the average exposure for the U.S. population (custom subpopulations could not be calculated for chronic exposure). The ambient air exposure estimates for adults were used to estimate aggregate exposure. The ambient air exposure estimates were adjusted to 124, 15 and 11 ng/kg for acute, seasonal and chronic exposure, respectively, assuming a maximum exposure of 16 hours per day to residential air for agricultural workers. The acute aggregate exposures for workers ranged from 0.0030 mg/kg/day to 5.85 mg/kg/day. The seasonal aggregate exposure for ranged from 0.0016 mg/kg/day to 1.55 mg/kg/day The chronic aggregate exposure for workers ranged from 0.0006 mg/kg/day to 0.243 mg/kg/day. The lifetime aggregate exposure for workers ranged from 0.0003 mg/kg/day to 0.130 mg/kg/day. The dietary, drinking water and ambient air exposure was less than one percent of the aggregate exposure for most workers. Consequently, its addition will not quantitatively impact the aggregate exposure. Only for work activities where the occupational exposure was low (M/L/As using low-pressure handwands and field workers harvesting/thinning citrus) did the dietary, drinking water and ambient air represent a significant contribution. Even for these activities, the dietary, drinking water and ambient air exposure combined represented only 15% of the aggregate exposure.

Table 23. Estimated Aggregate Exposure Dosages for Methidathion in Agricultural Workers[a]

Exposure Scenarios	Acute mg/kg/day	Seasonal mg/kg/day	Chronic mg/kg/day	Lifetime mg/kg/day
Handlers				
Aerial				
M/L[b]	1.15	0.459	0.038	0.020
Applicator	4.65	1.55	0.129	0.069
Flagger	1.90	0.476	0.040	0.021
Airblast				
M/L	0.132	0.052	0.009	0.005
Applicator	5.85	1.46	0.243	0.130
Groundboom				
M/L	0.158	0.063	0.010	0.006
Applicator	0.176	0.044	0.007	0.004
Backpack sprayer				
M/L/A[c]	0.190	NA	NA	NA
Low-pressure handwand				
M/L/A	0.0038	NA	NA	NA
Field Workers				
Scouting in cotton/safflower	0.119	0.0216	0.0053	0.0028
Harvesting/thinning citrus	0.0030	0.0016	0.0006	0.0003
Thinning artichokes	0.018	0.0034	0.0008	0.0004

a Aggregate exposure estimates are the sum of the occupational exposure estimates from Table 21 and the dietary and drinking water estimates from Table 20 and ambient air estimates from Table 22. The acute dietary and drinking water estimates for workers was 293 ng/kg. The seasonal and chronic dietary and drinking water estimates for workers were 4 ng/kg/day based on the U.S. population. The ambient air exposure estimates were adjusted to 124, 15 and 11 ng/kg/day assuming workers are exposed to residential air for a maximum of 16 hours per day.

b M/L = Mixer/Loader

c M/L/A = Mixer/Loader/Applicator

General Public

The aggregate exposure to methidathion through the diet, drinking water and residential (ambient) air was considered in the potential exposure for the general public. The estimated acute combined dietary and drinking water exposure to methidathion was assumed to be 1.067 and 0.293 µg/kg/day for children (ages 1-6/child population with highest acute dietary exposure) and adults (U.S. population), respectively. Since no seasonal exposure was estimated for dietary and drinking water exposure, the chronic dietary and drinking water exposures were used estimating seasonal aggregate exposure. The estimated chronic dietary and drinking water exposure was assumed to be 0.014 and 0.004 µg/kg/day for children (non-nursing infants less than 1 year old/child populations with the highest chronic dietary exposure) and adults (U.S. populations), respectively. The application site air exposure from Table 22 was used for the residential air exposure in the acute aggregate exposure for children and adults. The ambient air exposure from Table 22 was used for the residential air exposure in the seasonal and chronic aggregate exposure estimates. The acute aggregate exposure for children and adults was 1.46

and 0.557 μg/kg, respectively. The seasonal aggregate exposure for children and adults was 0.061 and 0.026 μg/kg/day, respectively. The chronic aggregate exposure for children and adults was 0.049 and 0.021 μg/kg/day, respectively.

C. RISK CHARACTERIZATION

The risk for non-oncogenic human health effects is expressed as a margin of exposure (MOE). The MOE is the ratio of the NOEL from experimental animal studies to the human exposure dosage.

$$\textit{Margin of Exposure} = \frac{\textit{NOEL}}{\textit{Exposure Dosage}}$$

The risk for oncogenic effects was calculated by multiplying the oncogenic potency by the exposure dosage.

$$\textit{Oncogenic Risk} = \textit{Oncogenic Potency} \ x \ \textit{Exposure Dosage}$$

Dietary

The MOEs for dietary exposure to methidathion were calculated for the various population subgroups using the NOEL for acute toxicity (0.3 mg/kg) and the acute dietary exposure dosages (Table 24). With the Tier 1 analysis, the MOEs for acute toxicity ranged from 280 for nursing infants less than one year old to 1,200 for males 20 years and older.

The MOEs for chronic dietary exposure to methidathion were calculated for the various population subgroups using the NOEL for chronic toxicity (0.15 mg/kg/day) and the chronic dietary exposure dosages (Table 24). In the Tier 1 analysis, the chronic MOEs ranged from 1,500 for children 1 to 6 years old to 7,000 for males 20 years and older. Replacement of PDP residue data for a few critical commodities in the Tier 2 analysis increased the chronic MOEs to 3,400 for non-nursing infants less than one year old up to 15,000 for both non-pregnant, non-nursing females 20 years and older and seniors 55 years and older. Adjustment of chronic dietary exposure based on available PCT data in the Tier 3 analysis increased the chronic MOEs even further to 8,200 for non-nursing infants up to 49,000 for non-pregnant, non-nursing females 13 years and older. After elimination of the secondary residues in the Tier 4 analysis, the chronic MOEs ranged from 15,000 for non-nursing infants less than one year old to 96,000 for non-pregnant, non-nursing females 13 to 19 years old.

The estimated oncogenic risk from dietary exposure was calculated using the chronic exposure for the U.S. population and the oncogenic potency. In the Tier 1 analysis, the estimated oncogenic risk from dietary exposure to methidathion ranged from 1.2×10^{-5} (MLE) to 1.8×10^{-5} (95% UB). With use of PDP data for a few critical commodities in the Tier 2 analysis, the estimated oncogenic risk decreased to 5.2×10^{-6} for the MLE and 8.1×10^{-6} for the 95% UB.

Table 24. Estimated Margins of Exposure for Potential Acute and Chronic Dietary Exposure to Methidathion for Selected Population Subgroups

Population Subgroup	Margins of Exposure[a]				
	Acute	Chronic			
	Tier 1	Tier 1	Tier 2	Tier 3	Tier 4
U.S. Population	720	4,400	9,800	33,000	55,000
Western Region	650	4,100	9,700	30,000	46,000
Nursing Infants (< 1 yr)	280	3,300	8,800	41,000	63,000
Non-nursing Infants (< 1 yr)	350	1,900	3,400	8,200	15,000
Children (1-6 yrs)	290	1,500	3,900	13,000	25,000
Children (7-12 yrs)	530	2,700	5,700	20,000	33,000
Females (13+ yrs/P/NN)	840	4,700	11,000	32,000	49,000
Females (13+ yrs/N)	600	3,500	8,000	22,000	28,000
Females (13-19 yrs/NP/NN)	840	5,400	13,000	49,000	96,000
Females (20+ yrs/NP/NN)	1,100	6,500	15,000	49,000	72,000
Males (13-19 yrs)	800	4,600	10,000	36,000	68,000
Males (20+ yrs)	1,200	7,000	14,000	47,000	72,000
Seniors (55+ yrs)	1,100	6,500	15,000	46,000	65,000
Workers (16+ yrs)	1,100	NA	NA	NA	NA

a Margin of Exposure = NOEL / Exposure Dosage. Acute NOEL = 0.3 mg/kg (male rats, reduced ChE activity in cerebral cortex). Chronic NOEL = 0.15 mg/kg/day (dogs, elevated liver enzymes in serum and histological lesions in the liver). Exposure dosages from Table 19. Values rounded to two significant figures.

P Pregnant

NN Not Nursing

N Nursing

NP Not pregnant

NA Not available. The TAS Exposure-1™ program does not calculate an exposure estimate for customized population subgroups, such as, workers 16 years and older.

Adjustment for PCT in the Tier 3 analysis, reduced the estimated oncogenic risk further to 1.6 x 10^{-6} for the MLE and 2.4 x 10^{-6} for the 95% UB. Elimination of the secondary residues in the Tier 4 analysis, resulted in an estimated oncogenic risk between 9.4 x 10^{-7} for the MLE and 1.5 x 10^{-6} for the 95% UB.

Drinking Water

The acute MOEs for drinking water exposure to methidathion are summarized in Table 25. The acute MOEs for drinking water ranged from 1,700 for non-nursing infants less than one year old to 10,000 for non-pregnant, non-nursing females 13 to 19 years old. The MOEs for combined drinking water and dietary exposure to methidathion are also summarized in Table 25. The acute MOEs for combined exposure ranged from 280 for children 1 to 6 years old to 1,100 for both males 20 years and older and seniors 55 years and older.

The chronic MOEs for drinking water exposure to methidathion are summarized in Table 25. The chronic MOEs for drinking water ranged from 38,000 for non-nursing infants less than one year old to 230,000 for non-pregnant, non-nursing females 13 to 19 years old. The MOEs for combined drinking water and dietary exposure to methidathion are also summarized in Table 25. The acute MOEs for combined exposure ranged from 11,000 for non-nursing infants less than one year old to 68,000 for non-pregnant, non-nursing females 13 to 19 years old.

The estimated oncogenic risk from exposure to methidathion in drinking water was calculated using the chronic water exposure for the U.S. population (1 ng/kg/day) and the adjusted oncogenic potency. The estimated oncogenic risk for drinking water exposure alone ranged from 2.9×10^{-7} (MLE) to 4.5×10^{-7} (95% UB). When drinking water exposure was combined with dietary exposure in the Tier 4 analysis, the estimated oncogenic risk ranged from 1.2×10^{-6} (MLE) to 1.9×10^{-6} (95% UB).

Occupational

The acute MOEs for occupational exposure to methidathion were calculated using the NOEL for acute toxicity (0.3 mg/kg) and the ADDs in Table 21. The MOEs for acute exposure ranged from < 1 for airblast applicators to 110 for harvesting and thinning of citrus (Table 26).

The seasonal MOEs for occupational exposure to methidathion were calculated using the subchronic NOEL (0.2 mg/kg/day) and the SADDs in Table 21. The MOEs for seasonal exposure ranged from < 1 for aerial applicators to 140 for harvesting and thinning of citrus (Table 26).

The MOEs for chronic occupational exposure to methidathion were calculated for the various exposure scenarios using the NOEL for chronic toxicity (0.15 mg/kg/day) and the AADDs in Table 21. The chronic MOEs ranged from < 1 for airblast applicators to 250 for harvesting and thinning of citrus (Table 26).

The oncogenic risk for agricultural workers exposed to methidathion was calculated using the LADDs in Table 21. The estimated oncogenic potency of methidathion based on the incidence of liver hepatocellular adenomas and carcinomas in male mice ranged from 0.34 (MLE) to 0.53 (95% UB) $(mg/kg/day)^{-1}$. The estimated oncogenic risk for agricultural workers

Table 25. Estimated Margins of Exposure for Potential Acute and Chronic Drinking Water Exposure to Methidathion for Selected Population Subgroups

Population Subgroup	Margin of Exposure[a]			
	Acute		Chronic	
	Water	Water + Diet[b]	Water	Water + Diet[c]
U.S. Population	7,200	680	180,000	42,000
Western Region	6,500	620	180,000	37,000
Nursing Infants (< 1 yr)	4,800	340	180,000	46,000
Non-nursing Infants (< 1 yr)	1,700	330	38,000	11,000
Children (1-6 yrs)	4,900	280	120,000	20,000
Children (7-12 yrs)	7,200	520	170,000	28,000
Females (13+ yrs/P/NN)	9,200	810	210,000	40,000
Females (13+ yrs/N)	8,200	560	180,000	24,000
Females (13-19 yrs/NP/NN)	10,000	800	230,000	68,000
Females (20+ yrs/NP/NN)	8,700	1,000	190,000	52,000
Males (13-19 yrs)	9,100	770	220,000	52,000
Males (20+ yrs)	9,100	1,100	210,000	53,000
Seniors (55+ yrs)	9,700	1,100	200,000	49,000
Workers (16+ yrs)	8,900	1,000	NA	NA

a Margin of Exposure = NOEL / Exposure Dosage. Acute NOEL = 0.3 mg/kg (male rats, reduced ChE activity in cerebral cortex). Chronic NOEL = 0.15 mg/kg/day (dogs, elevated liver enzymes in serum and histological lesions in the liver). Exposure dosages from Table 20. Values rounded to two significant figures.
b Acute dietary exposure based on residues used in Tier 1 analysis.
c Chronic dietary exposure based on residues used in Tier 4 analysis.
P Pregnant
NN Not Nursing
N Nursing
NP Not pregnant
NA Not available. The TAS Exposure-1™ program does not calculate an exposure estimate for customized population subgroups, such as, workers 16 years and older.

Table 26. Margins of Exposure for Agricultural Workers Exposed to Methidathion[a]

Exposure Scenarios	Acute	Seasonal	Chronic
Handlers			
Aerial			
M/L[a]	< 1	< 1	4
Applicator	< 1	< 1	1
Flagger	< 1	< 1	4
Airblast			
M/L	2	4	17
Applicator	< 1	< 1	< 1
Groundboom			
M/L	2	3	15
Applicator	2	5	21
Backpack sprayer			
M/L/A[c]	2	NA	NA
Low-pressure handwand			
M/L/A	88	NA	NA
Field Workers			
Scouting in cotton/safflower	3	9	28
Harvesting/thinning citrus	110	140	250
Thinning artichokes	17	63	190

a Margin of Exposure = NOEL / Exposure Dosage. Acute NOEL = 0.3 mg/kg (male rats, cortex ChE inhibition). Seasonal NOEL = 0.2 mg/kg/day (rats, RBCs and brain regional ChE inhibition). Chronic NOEL = 0.15 mg/kg/day (dogs, elevated liver enzymes in serum and histological lesions in the lever). Exposure dosages from Table 21. Values rounded to two significant figures or the nearest whole number if less than 10.

b M/L = Mixer/Loader

c M/L/A = Mixer/Loader/Applicator

using the MLE for oncogenic potency ranged 1.0×10^{-4} to 4.4×10^{-2} (Table 27). When the 95% UB for oncogenic potency was used, the estimated oncogenic risk for workers ranged from 1.6×10^{-4} to 6.9×10^{-2}.

Ambient and Application Site Air

The MOEs for acute exposure to methidathion were calculated using the estimated acute NOEL from the acute neurotoxicity study in rats (0.3 mg/kg/day for cortex ChE inhibition) and the ADDs for application site and ambient air in Table 22. The MOEs for application site air ranged from 580 for children to 1,100 for adults (Table 28). The acute MOEs for ambient air ranged from 770 for children to 1,600 in adults. The MOEs for seasonal exposure to methidathion were calculated using the NOEL from the subchronic neurotoxicity study in rats (0.2 mg/kg/day for cortex ChE inhibition) and the SADDs for ambient air at the Jefferson Elementary School site from Table 22. The seasonal MOEs ranged from 4,300 for children to 9,100 for adults (Table 28). The MOEs for chronic exposure to methidathion were calculated using the chronic NOEL of 0.15 mg/kg/day based on elevated liver enzymes in serum and

Table 27. The Estimated Oncogenic Risk for Agricultural workers for Potential Lifetime Exposure to Methidathion[a]

Exposure Scenarios	Maximum Likelihood Estimate	95% Upper Bound
Handlers		
Aerial		
M/L	6.8×10^{-3}	1.1×10^{-2}
Applicator	2.3×10^{-2}	3.7×10^{-2}
Flagger	7.1×10^{-3}	1.1×10^{-2}
Airblast		
M/L	1.7×10^{-3}	2.7×10^{-3}
Applicator	4.4×10^{-2}	6.9×10^{-2}
Groundboom		
M/L	2.0×10^{-3}	3.2×10^{-3}
Applicator	1.4×10^{-3}	2.1×10^{-3}
Backpack sprayer		
M/L/A	NA	NA
Low-pressure handwand		
M/L/A	NA	NA
Field Workers		
Scouting in cotton/safflower	9.5×10^{-4}	1.5×10^{-3}
Harvesting/thinning citrus	1.0×10^{-4}	1.6×10^{-4}
Thinning of artichokes	1.4×10^{-4}	2.1×10^{-4}

a Oncogenic Risk = Oncogenic Potency x Exposure Dosage. The exposure dosage was the LADD in Table 21. The maximum likelihood estimate for oncogenic potency was 0.34 $(mg/kg/day)^{-1}$. The 95% upper bound estimate for oncogenic potency was 0.53 $(mg/kg/day)^{-1}$.

histological lesions in the liver in dogs and the AADDs for ambient air at the Jefferson site from Table 22. The MOEs for chronic exposure to methidathion in ambient air ranged from 4,300 for children to 8,800 for adults (Table 28). The oncogenic risk was calculated using the AADD for adults for ambient air at the Jefferson site (7 ng/kg/day) and the estimated oncogenic potency based on liver hepatocellular adenomas and carcinomas in male mice (0.34 $(mg/kg/day)^{-1}$ for MLE or 0.54 $(mg/kg/day)^{-1}$ for 95% UB). The estimated oncogenic risk from lifetime exposure to ambient air at the Jefferson site ranged from 5.8×10^{-6} (MLE) to 9.0×10^{-6} (95% UB).

Aggregate Exposure

The acute aggregate MOEs for agricultural workers were calculated using the acute aggregate exposure estimates in Table 23 and the estimated NOEL from the rat acute neurotoxicity study (0.3 mg/kg). Since dietary, drinking water and residential air exposure contributed less than 1% to the aggregate exposure for most agricultural workers, the aggregate MOEs were not significantly different from the occupational MOEs for most workers (Table 29). The exceptions were MLAs using low-pressure handwands and field workers doing harvesting and thinning of citrus. The acute aggregate MOEs were 79 for MLAs using low-pressure

Table 28. Estimated Margins of Exposure for Potential Offsite and Ambient Air Exposure to Methidathion for the General Public[a]

Exposure Scenarios	Children	Adults
Application Site		
Acute	580	1,100
Ambient		
Acute	770	1,600
Seasonal	4,300	9,100
Chronic	4,300	8,800

a Margin of Exposure = NOEL / Exposure Dosage. Acute NOEL = 0.3 mg/kg (male rats, cortex ChE inhibition). Seasonal NOEL = 0.2 mg/kg/day (rats, RBCs and brain regional ChE inhibition). Chronic NOEL = 0.15 mg/kg/day (dogs, elevated liver enzymes in serum and histological lesions in the lever). Exposure dosages from Table 22. Values rounded to two significant figures.

Table 29. Margins of Exposure for Aggregate Exposure to Methidathion in Agricultural Workers[a]

Exposure Scenarios	Acute	Seasonal	Chronic
Handlers			
Aerial			
M/L[a]	< 1	< 1	4
Applicator	< 1	< 1	1
Flagger	< 1	< 1	4
Airblast			
M/L	2	4	17
Applicator	< 1	< 1	< 1
Groundboom			
M/L	2	3	15
Applicator	2	5	21
Backpack sprayer			
M/L/A[c]	2	NA	NA
Low-pressure handwand			
M/L/A	79	NA	NA
Field Workers			
Scouting in cotton/safflower	3	9	28
Harvesting/thinning citrus	100	120	250
Thinning artichokes	17	59	190

a Margin of Exposure = NOEL / Exposure Dosage. Acute NOEL = 0.3 mg/kg (male rats, cortex ChE inhibition). Seasonal NOEL = 0.2 mg/kg/day (rats, RBC and brain regional ChE inhibition). Chronic NOEL = 0.15 mg/kg/day (dogs, elevated liver enzymes in serum and histological lesions in the lever). Exposure dosages from Table 23. Values rounded to two significant figures or the nearest whole number if less than 10.

b M/L = Mixer/Loader

c M/L/A = Mixer/Loader/Applicator

handwands and 100 for field workers harvesting/thinning citrus. The MOEs for seasonal aggregate exposure were calculated using the aggregate seasonal exposure estimates in Table 23 and the subchronic NOEL from the subchronic neurotoxicity study in rats (0.2 mg/kg/day). Among agricultural workers, only the MOEs for two field worker scenarios were quantitatively different from the MOEs for occupational exposure alone. The seasonal aggregate MOEs were 125 for harvesting/thinning of citrus and 59 for thinning of artichokes (Table 29). The MOEs for chronic aggregate exposure were calculated using the chronic exposure estimates in Table 23 and the chronic NOEL from the 1-year dog study (0.15 mg/kg/day). This time there was no quantitative impact on the chronic MOEs when occupational exposure was aggregated with dietary, drinking water and ambient air exposure even for field workers (Table 29).

The aggregate oncogenic risk for agricultural workers exposed to methidathion was calculated using the lifetime exposure estimates in Table 23. The estimated oncogenic potency of methidathion based on the incidence of liver hepatocellular adenomas and carcinomas in male mice ranged from 0.34 (MLE) to 0.53 (95% UB) $(mg/kg/day)^{-1}$. The estimated aggregate oncogenic risk for agricultural workers were not significantly different from the estimated oncogenic risk from occupational exposure alone (Table 30).

Table 30. The Estimated Aggregate Oncogenic Risk for Agricultural Workers for Potential Lifetime Exposure to Methidathion[a]

Exposure Scenarios	Maximum Likelihood Estimate	95% Upper Bound
Handlers		
Aerial		
M/L	6.8×10^{-3}	1.1×10^{-2}
Applicator	2.3×10^{-2}	3.7×10^{-2}
Flagger	7.1×10^{-3}	1.1×10^{-2}
Airblast		
M/L	1.7×10^{-3}	2.7×10^{-3}
Applicator	4.4×10^{-2}	6.9×10^{-1}
Groundboom		
M/L	2.0×10^{-3}	3.2×10^{-3}
Applicator	1.4×10^{-3}	2.1×10^{-3}
Backpack sprayer		
M/L/A	NA	NA
Low-pressure handwand		
M/L/A	NA	NA
Field Workers		
Scouting in cotton/safflower	9.5×10^{-4}	1.5×10^{-3}
Harvesting/thinning citrus	1.0×10^{-4}	1.6×10^{-4}
Thinning of artichokes	1.4×10^{-4}	2.1×10^{-4}

a Oncogenic Risk = Oncogenic Potency x Exposure Dosage. The exposure dosage was the LADD in Table 23. The maximum likelihood estimate for oncogenic potency was 0.34 $(mg/kg/day)^{-1}$. The 95% upper bound estimate for oncogenic potency was 0.53 $(mg/kg/day)^{-1}$.

The aggregate MOEs for the general public were calculated using the aggregate exposure estimates for them presented in the Exposure Assessment section of this document (in text, no table) and the corresponding NOELs for acute, subchronic and chronic toxicity (0.3, 0.2 and 0.15 mg/kg/day, respectively). The acute aggregate MOEs were 210 and 540 for children and adults, respectively. The seasonal aggregate MOEs were 3,300 for children and 7,700 for adults. The chronic aggregate MOEs were 3,100 and 7,200 for children and adults, respectively. The aggregate oncogenic risk for the general public was calculated using the chronic aggregate exposure estimate for adults and the estimated oncogenic potency based on liver hepatocellular adenomas and carcinomas in male mice (0.34 $(mg/kg/day)^{-1}$ for MLE or 0.54 $(mg/kg/day)^{-1}$ for 95% UB). The aggregate oncogenic risk for the general public was estimated to be between 7.1×10^{-6} (MLE) and 1.1×10^{-5} (95% UB).

IV. RISK APPRAISAL

Introduction

Risk assessment is the process used to evaluate the potential for human exposure and the likelihood that the adverse effects observed in toxicity studies with laboratory animals will occur in humans under the specific exposure conditions. Every risk assessment has inherent limitations on the application of existing data to estimate the potential risk to human health. Therefore, certain assumptions and extrapolations are incorporated into the hazard identification, dose-response assessment, and exposure assessment processes. These, in turn, result in uncertainty in the risk characterization which integrates all the information from the previous three processes. Qualitatively, risk assessments for all chemicals have similar uncertainties. However, the degree or magnitude of the uncertainty can vary depending on the availability and quality of the data, and the types of exposure scenarios being assessed. Specific areas of uncertainty associated with this risk assessment for methidathion are delineated in the following discussion.

Hazard Identification

The primary mechanism of toxicity for methidathion is the inhibition of AChE in the nervous system. Consequently, brain ChE inhibition was considered an adverse effect for methidathion. In an acute neurotoxicity study, reduced ChE activity was seen in the cerebral cortex of male rats (59% of control activity) at the time to peak effect at the lowest dose tested, 1 mg/kg (Chang and Richter, 1994). However, no clinical signs or changes in behavior were seen in the FOB until 8 mg/kg. At 8 mg/kg, clinical signs and behavioral signs were seen in both sexes, although they were more pronounced in females. The reduction in ChE activity in the different regions of the brain were also more pronounced in females (8-25% of controls) than males (16-32% of controls) at 8 mg/kg. Since a NOEL was not observed for reduced ChE activity in the cerebral cortex of males, it was estimated by a dividing the LOEL by an uncertainty factor. A smaller uncertainty was selected to estimate the NOEL because the severity of the endpoint was considered mild for the following reasons: 1) no significant blood ChE inhibition was seen at the LOEL; 2) only one region of the brain in one sex was affected at the LOEL; 3) the cortex was not uniquely sensitive to ChE inhibition at higher doses; 4) statistically significant increases in neurological signs were not observed in the functional observational battery in either sex until 8 mg/kg; and 5) males were not more sensitive than females based on neurological signs or regional brain ChE inhibition at higher dose levels. Furthermore, a NOEL of 0.2 mg/kg/day was observed for the same endpoint in the 90-day subchronic neurotoxicity study for methidathion. A benchmark dose (BMD) analysis of the data using U.S. EPA's Benchmark Dose Software (BMDS, version 1.3.2) also supported a smaller uncertainty factor. With continuous data such as ChE activity, the benchmark response (BMR) level used should depend on the normal variation anticipated in the data. U.S. EPA used a BMR of 10% brain ChE inhibition when doing their evaluation of the cumulative toxicity of OPs (U.S. EPA, 2001). This level appears reasonable for whole brain data based on the coefficients of variation (CVs) for whole brain ChE activity in control animals observed in DPR's database for OPs which were usually between 5-10% for whole brain. However, the CVs for regional brain

ChE activity were much higher in DPR's database, usually between 10 and 25%. One contributing factor to this higher variability may be the difficulty in precisely excising various brain regions. In this study, the CV for the ChE activity in the cortex of male control animals at the time to peak effect was 23%. Using 23% for the BMR in the Hill model, the lower limit on the BMD (BMDL) was 0.38 mg/kg based on the inhibition in the cortex of males. Therefore, the acute NOEL for methidathion was estimated by dividing by an uncertainty factor of 3. This resulted in an estimated acute NOEL of 0.3 mg/kg which was only slightly higher than the subchronic NOEL (0.2 mg/kg/day) and the chronic NOEL (0.15 mg/kg/day).

A similar pattern of reduced brain ChE activity in the cerebral cortex was also seen in male rats (74-75% of control activity) at 10 ppm (0.6 mg/kg/day) in a 90-day neurotoxicity study (Chow and Turnier, 1995). The reduction was seen at 4 different time points, including 2, 4, 8 and 13 weeks, although it was only statistically significant at 2 and 4 weeks. It was the repetition of this effect in males at all 4 time points, that convinced the DPR toxicologists that this effect was treatment-related. Although clearly treatment related, the toxicological significance of the ChE inhibition in the cerebral cortex of males remains uncertain given that the females were the only ones exhibiting clinical signs or neurological effects in the FOB at 100 ppm (7.2 mg/kg/day). In a human health risk assessment, U.S. EPA used the reduced plasma, RBC and brain ChE activity at 2 weeks for their critical endpoint for estimating the acute RfD for methidathion with a NOEL of 0.2 mg/kg/day (Travaglini, 1999). If DPR had estimated their acute MOEs using this endpoint, the MOEs would be one-third lower than estimated.

The study selected for evaluating chronic dietary exposure to methidathion was a 1-year dog study (Chang and Walberg, 1991). The NOEL for this study was 4 ppm (0.15 mg/kg/day) based on elevated levels of liver enzymes (alkaline phosphatase, aspartate aminotransferase, alanine aminotransferase, sorbitol dehydrogenase) in the serum, dark red liver discoloration, cholestasis and mild chronic inflammation of the liver in both sexes at 40 ppm (M: 1.33 mg/kg/day; F: 1.39 mg/kg/day). A similar NOEL (0.17) was observed in a rat study based on clinical signs (alopecia, chromorhinorrhea, hyperactivity, hypersensitivity to touch, and tremors), reduced body weights, reduced food and water consumption, reduced ChE activity in RBCs (M: 78%; F: 82% of controls) and brain (F: 49%; M: 48% of controls), reduced liver weights, and skin lesions. Both studies were of acceptable quality, so this could not be used as the basis for selecting one study over the other. Differences in species sensitivity was also not clear. Rats were more sensitive to the neurotoxicity than dogs, but less sensitive to the hepatotoxicity. Therefore, the study with the lower NOEL was selected. However, the difference in the NOELs was minor and if the NOEL from the rat study had been used, the chronic MOEs would only be 13% higher than estimated. U.S. EPA also used the same study and NOEL for calculating the RfD for methidathion in their risk assessment for methidathion, although they included RBC ChE inhibition along with hepatotoxicity as the endpoints of concern (Travaglini, 1999). FAO/WHO JMPR identified a NOEL of 0.1 mg/kg/day in estimating the acceptable daily intake (ADI) for methidathion based on a one-year study in dogs (Caris, 1992).

The U.S. EPA Guidelines for Carcinogen Risk Assessment recommends using a linear approach when the mode of action is not known (U.S. EPA, 2005). They also recommend using a benchmark dose as a point of departure from the observed data to do a linear extrapolation to the origin. If DPR had used this approach, the potency estimates would be similar to those obtained with the MULTI-WEIB model. The ED_{10} (benchmark dose with an estimated excess lifetime tumor incidence of 10%) and LED_{10} (lower limit on ED_{10}) were estimated to be 0.48 and 0.16 mg/kg/day, respectively, using Multi-stage model in the U.S. EPA's Benchmark Dose Software (BMDS, version 1.3.2). The slope or potency factors corresponding to the ED_{10} and LED_{10} were estimated to be 0.21 and 0.63 $(mg/kg/day)^{-1}$, respectively, by dividing the risk at these dose levels (10% or 0.1) by the dose. If there had been sufficient evidence to support a threshold mechanism a non-linear approach could have been used. In this case, the U.S. EPA guidelines recommend dividing the LED_{10} by the exposure dosage to calculate a margin of exposure for oncogenicity. It is interesting to note that the LED_{10}, 0.16 mg/kg/day, is similar to chronic NOEL that was used to calculate the chronic MOEs, although the LED_{10} is based on the human equivalent dose. Consequently, the MOEs for oncogenicity would be similar to chronic MOEs calculated based on hepatotoxicity. One problem with using the nonlinear approach for threshold mechanisms as suggested by U.S. EPA's cancer guidelines is that they have not suggested how large the MOE for oncogenicity should be to be considered adequate. However, Gaylor et al. (1999) have proposed that the LED_{10}/10,000 or an MOE of 10,000 would be adequate for irreversible adverse health effects, including nongenotoxic oncogenic effects. This proposal assumes the LED_{10} is equivalent to a LOAEL, so that an uncertainty factor of 10 is needed to extrapolate to a NOAEL. An additional uncertainty factor of 1,000 is recommended for interspecies extrapolation, intraspecies variation in susceptibility, and increased susceptibility for children. It should be noted that the chronic MOE for methidathion from combined dietary and drinking water exposure was greater than 40,000. The chronic MOEs for occupational exposure ranged from <1 to 250 with most less than 100. The chronic MOEs for ambient air exposure ranged from 4,300 (children) to 8,800 (adults).

Exposure Assessment

The dietary exposure assessment was based primarily on DPR monitoring data and tolerance values when no monitoring data were available. DPR monitoring data tends to exaggerate exposure because it does not take into consideration any losses due to washing, peeling, cooking or other processing of commodities. PDP monitoring data is more representative of the actual exposure because commodities are washed and peeled if normally consumed that way. PDP data was used for 4 high consumption commodities including juices for 2 commodities in the Tier 2 and higher dietary analyses. DPR monitoring data may also exaggerate exposure for commodities where no residues were detected because of the higher LOQ which is used for samples with non-detectable residues. The LOQ for the PDP data is often lower, especially for California samples. The lower LOQ is most important in the chronic exposure where the mean residue value is used for each commodity. When no residues are detected, ½ of the LOQ is used. The chronic dietary exposure was also probably overestimated since residue levels were only adjusted for PCT for 8 commodities. It was assumed that 100% of the crops were treated for the other commodities, although this is unlikely.

The acute dietary exposure assessment may have also been overestimated since point estimates were used for residues rather than probabilistic estimates. In most cases, the point estimate for acute exposure was the highest detected residue level, but in a few cases where there was a sufficient number of samples, the 95th percentile of the residue levels was used. The acute exposure estimates would have been lower if the 95th percentile residue level had been used for all commodities. In addition, the acute dietary exposure is probably overestimated because it was assumed that all the commodities which might have been treated with methidathion contained residues on the same day at the highest residue level or 95th percentile which is highly unlikely. However, these conservative assumptions for acute exposure are counterbalanced to some degree by the fact that residues were monitored on composite samples which tends to eliminate the extreme values that might be found on single serving pieces of fruit or vegetables.

Drinking water exposure was probably overestimated for people whose only source of drinking water is well water since no residues of methidathion were found in well water monitored in California. Even for people whose source of drinking water is from surface water, exposure may be exaggerated since it is uncertain if the residues would persist after standard water treatment.

The uncertainties in the occupational exposure assessment are discussed in more detail in the Exposure Appraisal section of the EAD (Beauvais, 2004). In this assessment, PHED data were used to estimate exposure which results in more uncertainty in the estimates than if chemical-specific data were used. To compensate for this uncertainty, the 90% upper confidence limit on the mean and 95th percentile were used to estimate seasonal and acute exposure, respectively. This is a new approach used by DPR and one of the main reasons DPR's occupational exposure estimates were significantly higher than U.S. EPA's for the same scenarios.

Ambient and application site air monitoring were used to evaluate the air exposure to methidathion in the general public. Air monitoring was conducted in Tulare County during June and July of 1991. These sites and time were selected based on their high use in this county during this time of year. It is unclear, however, how representative these sites were since applications of methidathion around these sites was not confirmed. Furthermore, sites were only monitored Monday through Thursday for 8 weeks so exposure could have been underestimated if applications occurred outside these times. On the other hand, since monitoring was conducted during a high-use time, annual exposures may have been overestimated.

Risk Characterization

Generally, an MOE of at least 100 is considered sufficiently protective of human health when the NOEL for an adverse effect is derived from an animal study. The MOE of 100 allows for humans being 10 times more sensitive than animals and for a 10-fold variation in sensitivity between the lower range of the normal distribution in the overall population and the sensitive subgroup (Dourson *et al.*, 2002). The acute MOEs for dietary exposure when based only on the DPR monitoring data were greater than 200 for all population subgroups. The chronic MOEs for dietary exposure were all greater than 1,000 for all population subgroups even using just the DPR monitoring data. The acute MOEs for drinking water were greater than 1,500 for all population subgroups. When combined with dietary exposure from the Tier 1 analysis, the acute MOEs were still greater than 200 for all populations subgroups. The chronic MOEs from drinking water exposure were greater than 30,000 for all population subgroups. After combination with the dietary exposure from the Tier 4 analysis, the chronic MOEs were still greater than 10,000. An maximum contaminant level (MCL) has not been established for methidathion in water (U.S. EPA, 1999). The acute, seasonal and chronic MOEs for occupational exposure were less than 100 for all scenarios, except for harvesting and thinning of citrus. The MOEs were less than 10 for most exposure scenarios and less than 1 for some scenarios (aerial handlers and airblast applicators). The MOEs for acute exposure to methidathion in application site air were greater than 500 for both children and adults. The MOEs for acute, seasonal and chronic exposure to methidathion in ambient air were also greater than 500 for both children and adults. All of these MOEs are greater than the benchmark of 100 and, therefore, do not indicate that mitigation is needed. However, some of these MOEs are low enough to meet the criteria for identifying methidathion as a toxic air contaminant since the MOEs are not 10-fold greater than the benchmark that is considered adequately protective of human health (California Code of Regulations, Title 3, Division 6, Section 6890).

An oncogenic risk level less than 10^{-6} is generally considered negligible. The estimated oncogenic risk from exposure to methidathion in drinking water is less than the negligible risk level. On the other hand, the upper bound estimate of oncogenic risk from dietary exposure to methidathion in the U.S. population was just slightly greater than the negligible risk level at 1.5×10^{-6}. The upper bound estimate of oncogenic risk from combined exposure to methidathion in water and food was even higher at 1.9×10^{-6}. However, the oncogenic risk from exposure to methidathion may have been overestimated by using a linear approach if a threshold mechanism is involved. Consequently, the oncogenic risk from dietary exposure may be acceptable given the limited evidence for a genotoxic mechanism. The oncogenic risk estimates for occupational exposure to methidathion all exceeded the negligible risk level. The estimated oncogenic risk based on the maximum likelihood estimate ranged from 10^{-2} to 10^{-4}. The upper bound estimates of oncogenic risk were between 10^{-1} and 10^{-4}. Airblast applicators had the highest oncogenic risk estimates. The oncogenic risk estimates for the general public based on the ambient air exposure ranged from 5.8×10^{-6} to 9.0×10^{-6} which is also above the negligible risk level. The oncogenic risk levels from ambient air exposure not only meet the criteria for identifying methidathion as a toxic air contaminant since they are not 10-fold below the negligible oncogenic risk level, but they also suggest that mitigation may be needed since they are above the negligible risk level.

U.S. EPA's Reregistration Eligibility Document for Methidathion

U.S. EPA completed a Human Health Risk Assessment for methidathion in December 1999 (Travaglini, 1999) . U.S. EPA evaluated dietary, drinking water and occupational exposure to methidathion using route-specific NOELs whenever possible. U.S. EPA estimated acute dietary exposure to methidathion using PDP data and a Monte Carlo analysis in their recent Human Health Risk Assessment for methidathion (Travaglini, 1999). At the 99.9th percentile, the acute dietary estimates ranged from 281 ng/kg/day for females 13 years and older to 1,280 ng/kg/day for nursing infants less than 1 year old. These estimates were much lower than the estimates DPR obtained for acute exposure with the Tier 1 analysis using the 95th percentile and point estimates from DPR monitoring data. U.S. EPA estimated the chronic dietary exposure to range from 40 ng/kg/day for females 13 years and older to 338 ng/kg/day for children 1 to 6 years old with adjustment for percent crop treated. Unlike acute exposure, U.S. EPA's chronic dietary estimates are higher than DPR's chronic exposure estimates, even when compared to the Tier 1 analysis.

For acute dietary and drinking water exposure, U.S. EPA used a NOEL of 0.2 mg/kg/day from the 90-day neurotoxicity study based on brain ChE inhibition observed at 2 weeks (Chow and Turnier, 1995). DPR used an estimated NOEL of 0.3 mg/kg from the acute neurotoxicity study in rats based on brain ChE inhibition for evaluating dietary exposure (Chang and Richter, 1994). For chronic dietary and drinking water exposure, U.S. EPA use a NOEL of 0.15 mg/kg/day from a 1-year chronic toxicity study in dogs based on RBC ChE inhibition, elevated liver enzymes and liver lesions (Chang and Walberg, 1991). DPR used the same dog study and NOEL for evaluating chronic dietary and drinking water exposure to methidathion. U.S. EPA did a probabilistic (Monte Carlo) analysis for acute dietary exposure whereas DPR did only a deterministic analysis with point estimates. With their highly refined analysis, U.S. EPA found the acute dietary MOEs did not exceed their level of concern even at the 99.9th percentile. DPR only used the 95th percentile since point estimates were used, but also found the MOEs were greater than 100. The chronic dietary analysis was similar between U.S. EPA and DPR, although DPR's analysis was slightly more refined. Both agencies found the chronic dietary MOEs were adequate.

U.S. EPA calculated Estimated Environmental Concentrations (EECs) for methidathion in drinking water using the SCI-GROW model for ground water and the PRIZM-EXAMS model for surface water (Travaglini, 1999). The ground and surface water EECs were 0.4 and 6 ppb, respectively, for acute exposure. For chronic exposure, the EECs were 0.4 and 0.6 ppb for ground and surface water, respectively. Although DPR considers methidathion a potential groundwater contaminant based on environmental fate studies submitted, no methidathion residues have been detected in well water monitored by DPR between 1989 and 1996. Therefore, no residues were assumed to be in ground water. Methidathion residues were detected in surface water monitoring by DPR and U.S. Geological Survey; however, U.S. EPA's EECs for surface water were significantly higher than the concentrations used by DPR for acute (0.654 ppb) and chronic (0.029 ppb) drinking water exposure based on surface water monitoring data.

U.S EPA used Drinking Water Levels of Comparison (DWLOCs) to evaluate risk for drinking water. A DWLOC is the concentration of pesticide that is acceptable as an upper limit taking into consideration the aggregate exposure from food, water and residential uses. A DWLOC may vary between population subgroups depending on water consumption patterns and body weights. They estimated the acute DWLOCs to vary from 7.2 to 59 ppb for various sensitive population subgroups. The estimated chronic DWLOCs ranged from 13 to 48 ppm for the sensitive population subgroups. In all subgroups, the EECs did not exceed the DWLOCs. DPR evaluated drinking water exposure by using surface water monitoring data collected in the state. The 95th percentile and mean of the surface water residues were evaluated separately and in combination with the dietary exposure for all population subgroups. The MOEs for drinking water exposure were all greater than 100, even when combined with dietary exposure.

U.S. EPA evaluated short-term dermal exposure in workers using a 21-day dermal toxicity study in rabbits conducted by Folinusz *et al.* (1986) with a NOEL of 20 mg/kg/day. DPR used the acute oral neurotoxicity study in rats to evaluate acute dermal and inhalation occupational exposure to methidathion with a NOEL of 0.3 mg/kg/day based on brain ChE inhibition (Chang and Richter, 1994). U.S. EPA selected the 90-day oral neurotoxicity study in rats for evaluating intermediate-term dermal and short and intermediate-term inhalation exposure to methidathion in workers with an estimated NOEL of 0.2 mg/kg/day based on plasma, RBC and brain ChE inhibition (Chow and Turnier, 1995). Because a route-specific NOEL was not used, U.S. EPA applied a dermal absorption factor of 30% or an inhalation absorption factor of 100% to the exposure dosage before calculating the MOEs. The dermal absorption was estimated by taking the ratio of the NOAELs from the oral developmental toxicity study in rabbits (6 mg/kg/day) and the 21-day dermal toxicity study in rabbits (20 mg/kg/day). DPR also used the 90-day neurotoxicity study in rats with the same NOEL for evaluating subchronic dermal and inhalation occupational exposure to methidathion. However, DPR assumed a default assumption of 50% dermal absorption and 100% inhalation absorption. U.S. EPA concluded that the current use pattern (1-2 applications/year) did not indicate a concern for potential long-term occupational exposure and, therefore, did not calculate any chronic MOEs. DPR concluded there was sufficient use throughout the year to calculate chronic MOEs for occupational exposure. U.S. EPA classified methidathion as a group C carcinogen (possible human carcinogen) based on the liver tumors in male mice, but did not consider the evidence strong enough to warrant a quantitative estimation of human risk. DPR did calculate oncogenic risk estimates for occupational exposure.

U.S. EPA calculated the occupational exposure for handlers using their Pesticide Handlers Exposure Database (PHED). DPR also used PHED to calculate exposure dosages for handlers. The same assumptions were made regarding the application rates, average body weight, average workday, acres applied per day. Despite using the same general method for calculating exposure, the ADDs calculated by U.S. EPA were lower than those calculated by DPR, primarily because DPR used the 90th upper confidence limit on the 95th percentile for the ADD, and the 90th upper confidence limit on the arithmetic mean for the SADD. U.S. EPA used only the geometric mean estimates for their ADDs to evaluate both short-term and intermediate-term exposure. For post-application occupational exposure, U.S. EPA used a similar formula to DPR's for calculating dermal exposure dosages from dislodgeable foliar residues (DFRs) and transfer factors (TFs); however, different DFRs and TFs were used. The DFRs and TFs varied depending on the REI used and the data from which the DFRs and TFs were derived. Consequently, different estimated dermal doses were calculated. U.S. EPA incorporated mitigation in their exposure assessment when MOEs were less than the target MOE of 100. However, in their 1999 risk assessment, U.S. EPA estimated the dermal MOEs were less than their target of 100 after mitigation for mixing/loading of liquid formulation for aerial application. The combined dermal and inhalation MOEs were less than 100 for mixing and loading of water soluble packets (WSPs) for aerial application and liquid aerial application with fixed-wing aircraft. U.S. EPA only considered changes in REIs in the mitigation for post-application exposure. The required REI that would result in an MOE greater than 100 varied from 1 day for early scouting in cotton fields to 24 days for citrus harvesting. DPR's exposure assessment only incorporated the protective equipment, engineering controls and REIs that are recommended in the current labels.

As part of the Food Quality Protection Act (FQPA), U.S. EPA evaluated the developmental and reproductive toxicity studies for methidathion and recommended the 10X uncertainty factor be reduced to 1X based on 1) completeness of the database, 2) no evidence of increased susceptibility in the developmental toxicity studies, 3) no evidence of increased susceptibility in the reproductive toxicity study, 4) no evidence for requiring a developmental neurotoxicity study in rats, 5) adequate residue data for evaluating dietary and drinking water exposure and 6) no residential use. DPR also concluded there was no evidence of increased pre- or post-natal sensitivity from the developmental and reproductive toxicity studies in rats and rabbits.

U.S. EPA completed an Interim Reregistration Eligibility Document (IRED) in March 2002 (U.S. EPA, 2002). There were no changes in the dietary and drinking water assessment from the 1999 risk assessment. The toxicity studies selected for evaluating short-term and intermediate-term occupational exposure also did not change. There were some slight changes in the exposure estimates based on different MOEs reported for the same tasks compared to their risk assessment from 1999. It is unclear what the basis was for these changes in the exposure estimates since the discussion of the exposure estimates was more brief than in the 1999 risk assessment and the exposure estimates were not reported. Regardless, U.S. EPA remained concerned about mixing and loading of WSPs for aerial application and liquid aerial application by fixed-wing aircraft. U.S. EPA proposed mitigating these risks by limiting the use of WSPs to non-aerial application, addition of PPE, use of closed systems and the application of minimum of 500 gallons of water per acre to dilute methidathion products. U.S. EPA recognizes these measures will not increase the MOEs to above 100 in all cases, but considers the remaining risks reasonable given protective assumptions in the risk assessment and considering the benefits of methidathion use.

Issues Related to the Food Quality Protection Act

The Food Quality Protection Act of 1996 mandated U.S. EPA to "upgrade its risk assessment process as part of the tolerance setting procedures" (U.S. EPA, 1997a and b). The improvements to risk assessment were based on the recommendations from the 1993 National Academy of Sciences report, "Pesticides in the Diets of Infants and Children" (NAS, 1993). The Act required an explicit finding that tolerances are safe for children. U.S. EPA was required to use an extra 10-fold safety factor to take into account potential pre- and post-natal developmental toxicity and the completeness of the data unless U.S. EPA determined, based on reliable data, that a different margin would be safe. In addition, U.S. EPA must consider available information on: 1) aggregate exposure from all non-occupational sources; 2) effects of cumulative exposure to the pesticide and other substances with common mechanisms of toxicity; 3) the effects of *in utero* exposure; and 4) the potential for endocrine disrupting effects.

Prenatal and Postnatal Sensitivity

Five developmental toxicity studies (3 with rats and 2 with rabbits) were available for methidathion. One rat and one rabbit study were acceptable based on FIFRA guidelines. Fetal effects included reduced ossification of the sternabrae and reduced body weights. The lowest developmental NOEL in an acceptable study was equal to or greater than 2.5 mg/kg/day, the highest dose tested in rats. There was no evidence of increased prenatal sensitivity to methidathion in any of these studies since the developmental NOELs were equal to or greater than the maternal NOELs. However, brain ChE activity was not measured in either adults or pups in any of the developmental toxicity studies.

Four reproductive toxicity studies in rats were available for methidathion with exposure ranging from one to three generations. Only one of these studies was found acceptable to DPR based on FIFRA guidelines. The effects observed in pups included tremors, signs of maternal neglect (cool to touch, starving, weak or lethargic), reduced pup weights and reduced survival. In the one acceptable study, the pup NOEL was the same as parental NOEL, 5 ppm (0.4 mg/kg/day). A comparison of the acute toxicity of methidathion in adult (> 90 days of age) and weanling (4-6 weeks of age) rats found weanling rats were slightly more sensitive to methidathion based on a slightly lower oral LD_{50} value (M: 21 mg/kg) than adults (M: 31 mg/kg; F: 32 mg/kg) (Gaines and Linder, 1986). Based on this evidence, there may be an increased postnatal sensitivity to methidathion. None of the reproductive toxicity studies nor the acute toxicity study conducted by Gaines and Linder (1986) measured brain ChE activity in either adults or pups.

Endocrine Effects

The Food Quality Protection Act (FQPA) of 1996 required U.S. EPA to develop a screening program to determine the endocrine disruption potential of pesticides. In 1997, the Risk Assessment Forum of the U.S. EPA published a report that reviewed the current state of science relative to environmental endocrine disruption (U.S. EPA, 1997c). U.S. EPA formed the Endocrine Disruptor Screening and Testing Advisory Committee (EDSTAC) to develop a strategy for screening and testing of pesticides for their potential to produce endocrine disruption. The EDSTAC members include various stakeholders and scientific experts. This screening and testing process is expected to be implemented by August of 1999 as required by FQPA.

Environmental chemicals can interact with the endocrine system, resulting in cancer, reproductive and/or developmental anomalies (EDSTAC, 1998). It may produce these effects by affecting hormonal production and synthesis, binding directly to hormone receptors or interfering with the breakdown of hormones (U.S. EPA, 1997c). The interim science policy stated in U.S. EPA's 1997 report is that "*the Agency does not consider endocrine disruption to be an adverse endpoint per se, but rather to be a mode or mechanism of action leading to other outcomes*." The only possible endocrine related effects in the available animal studies for methidathion were reduced mating index and poor maternal care (Salamon 1986 & 1987). However, it is unclear from this data if either of these effects are mediated through endocrine disruption, ChE inhibition or some other mechanism.

Cumulative Toxicity

There is a potential for cumulative toxicity between methidathion and other organophosphates (OPs) because they have a common mechanism of toxicity, inhibition of ChE. In fact, there is evidence that methidathion acted synergistically with at least 6 (carbaryl, mevinphos, azinphos-methyl, methyl parathion, fenchlorphos and disulfoton) out of 15 organophosphate compounds tested (Woodard Research, 1966a). Exposure to methidathion in the induction phase also resulted in a cross reaction when later challenged with DDVP, and naled, but not benomyl (Matsushita *et al.*, 1985). However, until recently, a scientifically defensible approach to quantitatively evaluate the potential for cumulative toxicity was not available. An elaborate methodology was recently developed by U.S. EPA to assess the exposure to multiple chemicals with a common mechanism of action (U.S. EPA, 2002b). Because the OPs were assigned priority for tolerance reassessment, they were the first to be considered as a "common mechanism group" for cumulative risk assessments. The U.S. EPA recently completed a preliminary cumulative risk assessment for the OPs (U.S. EPA, 2001). The assessment estimated the potential risk from exposure to multiple OPs by multiple pathways. A total of 31 OP pesticides were included in the risk assessment. These OPs were selected based on their detection in the USDA's PDP, as well as their potential for human exposure through residential, non-occupational uses and drinking water. The assessment utilized data from three exposure pathways: food, drinking water and residential/non-occupational exposure to OPs (air, soil, grass, indoor surfaces). Methidathion was one of the evaluated OPs in the food and drinking water exposure pathways.

U.S. EPA employed the relative potency factor (RPF) method to determine the combined exposure to the OPs. RPF was defined as the ratio of the toxic potency of a compound to that of an index chemical. Methamidophos was selected as the index chemical, because of the quality and extensive availability of its dose-response data for all routes of exposure. The toxic potencies for the OPs were based on the common endpoint of the inhibition of the brain ChE activity in female rats for 21 days or longer. Both the point of comparison among the chemicals and the point of departure (POD) for the index chemical was based on the BMD_{10}, the benchmark response of 10% reduction of the ChE activity. In this analysis, U.S. EPA considered the exposure to OP residues in foods as uniform across the U.S. Twelve regional assessments were conducted for drinking water and residential exposures. The uniform food exposure estimate was combined with region-specific exposures from residential uses and drinking water. In Region 7, which included California, the use of methidathion on apples, pears, peaches, apricots, nectarines, plums, almonds, walnuts, oranges, tomatoes and alfalfa was considered in the drinking water exposure modeling for the north and/or south central valley.

The conclusions from the preliminary OP cumulative risk assessment were that the drinking water is not a major contributor to the total risk. The exposures from OPs in food at percentiles above the 95^{th} percentile for all population subgroups were at least one order of magnitude higher than water. U.S. EPA indicated that additional sensitivity analysis is needed on the upper percentiles of the food exposure assessments before any risk management decisions can be made. U.S. EPA is in the process of developing guidelines for the application of the

FQPA factor for pre and post-natal sensitivity in the cumulative risk assessments for chemicals with a common mechanism of toxicity (U.S. EPA, 2002c).

Aggregate Exposure

The combined dietary, drinking water, occupational, and residential (ambient) air exposure for agricultural workers has been addressed in this document. The dietary, drinking water and ambient air exposure was less than one percent of the aggregate exposure for most workers. Consequently, its addition did not quantitatively impact the aggregate exposure. Only for work activities where the occupational exposure was low (e.g., M/L/As for low-pressure handwand and harvesting/thinning of citrus), did the dietary, drinking water and ambient air represent a significant contribution. Even for these activities, the dietary, drinking water and ambient air exposure represented less than 15% of the aggregate exposure.

The combined dietary, drinking water and ambient air exposure for the general public was also addressed in this document. The acute aggregate MOEs for the general public were all greater than 100. The seasonal and chronic aggregate MOEs were greater than 1,000. The aggregate oncogenic risk estimates for the general public were slightly higher than the negligible risk level, ranging from 7.1×10^{-6} to 1.1×10^{-5}. The ambient air exposure appears to be the primary contributor since the oncogenic risk estimates from ambient air exposure alone were also clearly greater than negligible risk level. Dietary exposure was also a significant contributor since the oncogenic risk estimates from dietary exposure alone were slightly greater than the negligible risk level. The drinking water exposure contributed the least to the aggregate exposure for the general population since drinking water exposure alone were slightly less than the negligible risk level.

V. TOLERANCE ASSESSMENT

A. INTRODUCTION

U.S. EPA

U.S. EPA is responsible under the Federal Food, Drug, and Cosmetic Act (FFDCA) for setting tolerances for pesticide residues in RACs (Section 408 of FFDCA) and processed commodities (Section 409 of FFDCA). A tolerance is the legal maximum residue concentration of a pesticide which is allowed on a raw agricultural commodity or processed food. The tolerances are established at levels necessary for the maximum application rate and frequency, and not expected to produce deleterious health effects in humans from chronic dietary exposure (U.S. EPA, 1991). The data requirements for tolerances include: (1) residue chemistry, (2) environmental fate, (3) toxicology, (4) product performance such as efficacy, and (5) product chemistry (Code of Federal Regulations, 1996). The field studies must reflect the proposed use with respect to the rate and mode of application, number and timing of applications and formulations proposed (U.S. EPA, 1982).

In 1996, the Food Quality Protection Act (FQPA) amended the overall regulation of pesticide residues under FIFRA and FFDCA (U.S. EPA, 1997a and b). One major change was the removal of the Delaney Clause that prohibited residues of cancer-causing pesticides in processed foods. The tolerances must be health-based and the same standards are used to establish tolerances for both the RACs and their processed forms. FQPA required an explicit finding that tolerances are safe for children. U.S. EPA was required to use an extra 10-fold safety factor to take into account potential pre- and post-natal developmental toxicity and the completeness of the data unless U.S. EPA determined, based on reliable data, that a different margin would be safe. In addition, the evaluations of the tolerance must take into account: (1) aggregate exposure from all non-occupational sources, (2) effects from cumulative exposure to the pesticide and other substances with common mechanisms of toxicity, (3) effects of *in utero* exposure; and (4) potential for endocrine disrupting effects.

Under FQPA, U.S. EPA is also required to reassess all existing tolerances and exemptions from tolerances for both active and inert ingredients by 2006 (U.S. EPA, 1997d). Previously, U.S. EPA reassessed tolerances as part of its reregistration and Special Review processes. In the evaluation of tolerances, the U.S. EPA uses a tiered approach and the assessment includes all label-use commodities.

California

In California, U.S. EPA established tolerances are evaluated under the mandate of Assembly Bill 2161, generally referred to as the Food Safety Act (Bronzan and Jones, 1989). The Act requires DPR to conduct an assessment of dietary risks associated with the consumption of produce and processed food treated with pesticides. In these assessments, the tolerance for each specific commodity is evaluated individually and is discussed in the following sections.

For a pesticide registered for use on a large number of commodities, tolerance assessments are conducted for only a group of selected fruits and vegetables. Generally, commodities are selected from all the uses based on the potential for high levels of exposure. For a number of RACs, only the tolerances for the commodities on FDA's list of the 20 most frequently consumed fruits and vegetables consumed were examined. For methidathion, the tolerances for the following commodities were evaluated: oranges (2.0 ppm), lemons (2.0 ppm), grapefruit (2.0 ppm), apples (0.05 ppm), pears (0.05 ppm), peaches (0.05 ppm), plums (0.05 ppm), cherries (0.05 ppm), and apricots (0.05 ppm). These 9 tree fruit commodities were selected because of their high consumption rates. In addition, several tolerances for nut commodities (almonds - 0.05 ppm, walnuts - 0.05 ppm and sunflower seeds - 0.5 ppm) were evaluated where at least 5% of the U.S. population were consumers according to the 1989-1991 USDA CSFII data. Tolerances for potatoes, meat, milk, poultry and eggs were not evaluated since U.S. EPA indicated in their revised dietary assessment for methidathion that the tolerances for these commodities will be revoked during reregistration (U.S. EPA, 1998).

B. ACUTE EXPOSURE

An acute exposure assessment is conducted for each individual label-approved commodity at the tolerance. The TAS Exposure-4 software program and the 1989-1991 USDA CSFII data were used in this assessment. The acute tolerance assessment does not routinely address multiple commodities at the tolerance levels since the probability of consuming multiple commodities at the tolerance decreases as the number of commodities included in the assessment increases. The 95th percentile of user-day exposures for all specific population subgroups was used in evaluating the margins of exposure for the various population subgroups.

The acute MOEs for the 12 commodities analyzed are summarized in Table 31. For some commodities (lemons, grapefruit, almonds, walnuts, and sunflower seeds), there was no consumption reported in the 1989-1991 USDA CSFII data for nursing infants less than 1 year old. Since the number of nursing infants surveyed was small (153), it is uncertain if these commodities are consumed by this population subgroup. There was also either no or low consumption of these commodities by non-nursing infants less than 1 year old (less than 10 out of 453 non-nursing infants). Therefore, the estimates of the exposure at the 95th percentile are not reliable for these commodities in this population subgroup. The exposure estimates for several other commodities (oranges, peaches, cherries, plums and apricots) for nursing infants is also questionable because there were less than 10 consumers. Table 22 does not include the results of tolerance assessments for 4 commodities (tangerines, limes, nectarines, kiwi fruit) because the results were not considered reliable since less than 5% of the U.S. population were consumers according the 1989-1991 USDA CSFII data.

The MOEs were less than 100 for most population subgroups for oranges and grapefruit. For apples, the MOEs were less than 100 for nursing infants less than one year old. The tolerances for all the stone fruit and nut commodities resulted in MOEs greater than 100 for all population subgroups. Based on these analyses, the tolerances for citrus fruit and apples should be reviewed, especially the citrus fruit. In order to obtain MOEs of at least 100 for these commodities, the tolerances would need to be reduced to 0.15 ppm for citrus fruit and 0.03 ppm for pome fruit.

C. CHRONIC EXPOSURE

A chronic exposure assessment using residues equal to the established tolerances for individual or combinations of commodities has not been conducted because it is highly improbable that an individual would chronically consume single or multiple commodities with pesticide residues at the tolerance levels. This conclusion is supported by data from both federal and DPR (formerly CDFA) pesticide monitoring programs which indicate that less than one percent of all sampled commodities have residue levels at or above the established tolerance(DPR, 1993b, 1995b, 1996c & 1997b).

Table 31. Margins of Exposure for Acute Dietary Exposure to Tolerance Levels of Methidathion on Selected Raw Agricultural Commodities[a]

Population Subgroup	Oranges	Grapefruit	Lemons	Apples	Pears	Peaches
U.S. Population	22	20	410	470	890	1,500
Western Region	24	15	410	550	520	1,600
Nursing Infants (<1 yr)	1*	NC	NC	78	150*	580*
Non-Nursing Infants (<1 yr)	9	192*	1,100*	160	270	410
Children (1-6 yrs)	10	21	240	220	510	780
Children (7-12 yrs)	19	11	370	480	1,100	1,200
Females (13+ yrs/P/NN)	21	38	400	760	4,500	3,200
Females (13+ yrs/N)	30	21	390	370	1,400	2,000
Females (13-19 yrs/NP/NN)	33	16	370	910	1,200	2,000
Females (20+ yrs/NP/NN)	34	23	380	1,300	1,800	2,300
Males (13-19 yrs)	22	46	550	1,100	2,500	2,600
Males (20+ yrs)	40	18	520	1,500	2,300	2,500
Seniors (55+ yrs)	39	21	450	1,500	2,100	2,300

a Based on 95th exposure percentile for all user-day population subgroups. Values rounded to two significant figures.
NC There was no consumption of this commodity by this population subgroup in the 1989-1991 USDA Continuing Survey of Food Intakes by Individuals.
P Pregnant
NN Not nursing
N Nursing
NP Not pregnant
* Unreliable estimate of the 95th percentile of exposure since consumption based on less than 10 users.

Table 31 (cont.). Margins of Exposure for Acute Dietary Exposure to Tolerance Levels of Methidathion on Selected Raw Agricultural Commodities[a]

Population Subgroup	Plums	Cherries	Apricots	Almonds	Walnuts	Sunflower Seeds
U.S. Population	1,300	10,000	25,000	21,000	31,000	29,000
Western Region	1,500	9,800	8,500	19,000	32,000	23,000
Nursing Infants (<1 yr)	2,100*	3,500*	10,000*	NC	NC	NC
Non-Nursing Infants (<1 yr)	1,000	1,800	1,700	NC	15,000*	520,000*
Children (1-6 yrs)	860	7,200	16,000	16,000	26,000	4,800
Children (7-12 yrs)	770	14,000	35,000	25,000	26,000	16,000
Females (13+ yrs/P/NN)	1,000	21,000	20,000	140,000	35,000	13,000
Females (13+ yrs/N)	2,100	3,000	6,400	12,000	100,000	16,000
Females (13-19 yrs/NP/NN)	3,600	29,000	60,000	21,000	31,000	26,000
Females (20+ yrs/NP/NN)	1,500	16,000	19,000	29,000	29,000	30,000
Males (13-19 yrs)	1,700	20,000	51,000	22,000	46,000	110,000
Males (20+ yrs)	2,000	8,500	32,000	20,000	42,000	100,000
Seniors (55+ yrs)	1,700	11,000	9,200	40,000	32,000	170,000

a Based on 95th exposure percentile for all user-day population subgroups. Values rounded to two significant figures.
NC No consumption of this commodity by this population subgroup in the 1989-1991 USDA Continuing Survey of Food Intakes by Individuals.
P Pregnant
NN Not nursing
N Nursing
NP Not pregnant
* Unreliable estimate of the 95th percentile of exposure since consumption based on less than 10 users.

VI. REFERENCE CONCENTRATIONS

Air concentrations of methidathion below the reference concentrations (RfCs) are generally considered sufficiently low to protect human health. RfCs were calculated for methidathion for acute, seasonal and chronic exposures. The NOELs from oral studies were converted to equivalent human inhalation NOELs by dividing the oral NOELs by the respiratory rate for humans.

$$human\ inhalation\ NOEL\ (mg/m^3) = \frac{animal\ oral\ NOEL\ (mg/kg)}{respiratory\ rate_{human}\ (m^3/kg)}$$

Since children have the highest respiratory rate for humans relative to their body weight, their respiratory rate was used for humans. The resulting equivalent acute human inhalation NOEL was 0.51 mg/m^3 based on depressed ChE activity in the cerebral cortex of male rats (59% of controls), assuming a 24-hr default respiratory rate of 0.59 m^3/kg for children . The equivalent subchronic human inhalation NOEL was 0.34 mg/m^3 based on depressed ChE activity in the RBCs of both sexes (56-81%), in the cerebral cortex of male rats (74% of controls) and in the striatum (63% of controls) and hippocampus (76'% of controls) of female rats. The equivalent chronic human inhalation NOEL was 0.25 mg/m^3 based on elevated liver enzymes in the serum and histological lesions in the liver of dogs. Generally, the RfCs are calculated by dividing the equivalent human inhalation NOELs by an uncertainty factor of 100 when based on a NOEL from an animal study to account for interspecies and intraspecies variation in susceptibility.

$$RfC\ (mg/m^3) = \frac{human\ inhalation\ NOEL\ (mg/m^3)}{uncerta\,inty\ \ factor\ (e.g.,100)}$$

$$RfC\ (ppm) = RfC\ (mg/m^3)\ x\ \frac{M.Vol.(24.5L\ @\ 25^c C)}{M.Wt.(302g)}$$

The resultant RfC for acute exposure (24-hour) is 5.1 µg/m^3 (0.41 ppb) based on reduction in ChE activity in the cerebral cortex of male rats. The 24-hour time weighted average air concentration of methidathion in the first 24 hours with application site monitoring was 0.88 µg/m^3 (71 ppt). The 95th percent upper bound estimate of the ambient air concentrations at the Jefferson site was 0.66 µg/m^3 (54 ppt). The RfC for seasonal exposure to methidathion is 3.4 µg/m^3 (0.27 ppb) based on reduced ChE activity in the RBCs of both sexes, in cerebral cortex of male rats, and in the striatum and hippocampus of female rats. The mean air concentration at the Jefferson site during the one-month monitoring period was estimated to be 86 ng/m^3 (7.0 ppt). The RfC for chronic exposure to methidathion is 2.5 µg/m^3 (0.21 ppb) based on elevated liver enzymes in the serum and histological lesions in the liver in dogs. Assuming the season for methidathion use lasts 9 months, the annual average air concentration at the Jefferson site would be 64 ng/m^3 (5.2 ppt).

The air concentration which corresponds to a negligible oncogenic risk level (i.e., 10^{-6}) for methidathion was calculated by first estimating the exposure dosage divided by the 95% UB estimate of oncogenic potency (0.53 $(mg/kg/day)^{-1}$). For methidathion, the exposure dosage corresponding to a negligible oncogenic risk is 19 ng/kg/day. Assuming a lifetime exposure is necessary to produce the oncogenic effect, the exposure dosage was converted to an air concentration by dividing by the estimated breathing rate for an adult male (0.28 m^3/kg/day). The air concentration below which there would be no regulatory concern for oncogenic effects is 68 ng/m^3 (5.5 ppt).

VII. CONCLUSIONS

The risks for potential adverse human health effects with dietary, drinking water, occupational and ambient air exposure to methidathion were evaluated. Generally, an MOE of at least 100 is considered sufficiently protective of human health when the NOEL for an adverse effect is derived from an animal study. The MOE of 100 allows for humans being 10 times more sensitive than animals and for a 10-fold variation in sensitivity between the lower distribution of the overall human population and the sensitive subgroup. An oncogenic risk level less than 10^{-6} is generally considered negligible.

The MOEs for acute dietary exposure to methidathion were greater than 200 for all population subgroups based on DPR monitoring data. The MOEs for chronic dietary exposure to methidathion were greater than 10,000 with use of PDP data, adjustment for percent crop treated and elimination of residues for animal products. The upper bound estimate of oncogenic risk from dietary exposure to methidathion in the U.S. population was slightly greater than the negligible risk level of 10^{-6} even with use of PDP data, adjustment for percent crop treated and elimination of residues from animal products. The acute dietary MOEs based on the tolerance for methidathion residues were greater than 100 for all population subgroups on various commodities, except for citrus fruit and apples. The tolerance levels for these commodities, especially citrus fruit, should be reevaluated.

The MOEs for acute exposure to methidathion in drinking water were greater than 1,000 for all population subgroups based on DPR and U.S. Geological Survey monitoring data for surface water in California. The MOEs for chronic drinking water exposure to methidathion were greater than 30,000. The estimated oncogenic risk from exposure to methidathion in drinking water was less than the negligible risk level of 10^{-6}. When dietary and drinking water exposures were combined, the acute and chronic MOEs were still greater than 200 and 10,000, respectively, for all population subgroups. Addition of the drinking water exposure to dietary exposure, increased the upper bound estimate for oncogenic risk only slightly since the contribution from dietary exposure was so much greater.

The MOEs for acute, seasonal and chronic occupational exposure to methidathion were less than 100 for all exposure scenarios, except harvesting and thinning of citrus. The MOEs were less than 10 for most exposure scenarios and less than 1 for some scenarios (aerial handlers and airblast applicators). The oncogenic risk estimates for occupational exposure to methidathion all exceeded the negligible risk level. The estimated oncogenic risk based on the maximum likelihood estimate ranged from 10^{-2} to 10^{-4}. The upper bound estimates of oncogenic risk were between 10^{-1} and 10^{-4}. Airblast applicators had the highest oncogenic risk estimates.

The MOEs for acute exposure to methidathion in application site air were greater than 500 for both children and adults. The MOEs for acute, seasonal and chronic exposure to methidathion in ambient air were greater than 500 for both children and adults. These MOEs are sufficiently high that mitigation is not indicated, but are sufficiently low to meet the criteria for identifying methidathion as a toxic air contaminant. The oncogenic risk estimates for the general public based on the ambient air exposure ranged from 6 to 9 x 10^{-6} which is above the negligible risk level and may indicate mitigation is needed. This oncogenic risk level also meets the criteria for identification of methidathion as a toxic air contaminant since the exposure levels are not 10-fold below the negligible oncogenic risk level.

Aggregate exposure for agricultural workers and the general public did not dramatically increase the risk estimates for these groups. The MOEs for most agricultural workers were already significantly less than 100 without adding in additional exposure from diet, drinking water and ambient air. The aggregate MOEs for the general public were adequate for all exposure durations; however, the aggregate oncogenic risk estimates slightly exceeded the negligible risk level. The ambient air exposure appears to be the primary contributor since the oncogenic risk estimates from ambient air exposure alone were clearly greater than negligible risk level. Dietary exposure is also an important contributor since oncogenic risk estimates from dietary exposure alone also were slightly greater than the negligible risk level. Drinking water exposure appears to be the smallest contributor since the oncogenic risk estimates from drinking water alone were less than the negligible risk level.

VIII. REFERENCES

Allon, N., L. Raveh, E. Gilat, E. Cohen, J. Grunwald, and Y. Ashani, 1998. Prophylaxis against soman inhalation toxicity in guinea pigs by pretreatment alone with human serum butyrylcholinesterase. Toxicol. Sci. 43: 121-128.

Arni, P., 1980a. Salmonella/mammalian-microsome mutagenicity test with GS 13005. Ciba-Geigy Corp. DPR Vol. 298-003, Rec. No. 936024.

Arni, P., 1980b. Salmonella/mammalian-microsome mutagenicity test with GS 13005. Ciba-Geigy Corp. DPR Vol. 298-003, Rec. No. 936025.

Arni, P., 1980c. Intrasanquine host-mediated assay with S. typhimurium with GS 13005. Ciba-Geigy Corp. DPR Vol. 298-003, Rec. No. 936026.

Arni, P., 1980d. Salmonella/mammalian-microsome mutagenicity test with GS 12956. Ciba-Geigy Corp. DPR Vol. 298-003, Rec. No. 936022.

Arni, P., 1980e. Salmonella/mammalian-microsome mutagenicity test with GS 28730. Ciba-Geigy Corp. DPR Vol. 298-003, Rec. No. 936018.

Arni, P., 1980f. Salmonella/mammalian-microsome mutagenicity test with GS 28369. Ciba-Geigy Corp. DPR Vol. 298-003, Rec. No. 936023.

Arni, P. and D. Muller, 1981. Mutagenicity test on *Saccharomyces cerevisiae* MP-1 in vitro with GS 13005 (Test for mutagenic properties in yeast cells). Ciba-Geigy Corp. Cited In: Caris, M. (Health and Welfare Canada), 1993. Methidathion (evaluation for acceptable daily intake). In: Pesticide Residues in Food - 1992. Toxicology Evaluations. World Health Organization, Geneva. pp. 233-265.

Albanese, E.J. (Industrial Bio-Test Laboratories, Inc.), 1976. 28-Day range-finding study with Supracide® technical in albino mice. Ciba-Geigy Corp. DPR Vol. 298-016, Rec. No. 935983.

Ballard, C.G. and E.K. Perry, 2003. The role of butyrylcholinesterase in Alzheimer's disease. *In:* Butyrylcholinesterase: It's function and inhibitors (E. Giacobini, ed.). London: Martin Dunitz. pp. 123-134.

Bartkowiak, D.J. and B.W. Wilson, 1995. Avian plasma carboxylesterase activity as a potential biomarker of organophosphate pesticide exposure. Environ. Toxicol. Chem. 14(2): 2149-2153.

Beauvais, S., 2004. Estimation of Exposure of Persons in California to Pesticide Products That Contain Methidathion. Worker Health and Safety Branch, Department of Pesticide Regulation, California Environmental Protection Agency. HS-1805. June 4, 2004.

Bennett, K., 1997. Preliminary results of acute and chronic toxicity testing of surface water monitored in the San Joaquin River, winter 1996-1997. Memorandum to Don Weaver, Environmental Monitoring and Pest Management Branch, Department of Pesticide Regulation, California Environmental Protection Agency, Sacramento, CA. June 6, 1997.

Brimijoin, S. 1992. Enzymology and biology of cholinesterases. Proceedings of the U.S. EPA Workshop on Cholinesterase Methodologies. Office of Pesticide Programs, U.S. Environmental Protection Agency.

Brimijoin, S. and C. Koenigsberger, 1999. Cholinesterases in neural development: New findings and toxicologic implications. Environ. Health Persp. 107(Suppl. 1): 59-64.

Bronzan and Jones, 1989. Assembly Bill 2161, Addition to the Food and Agriculture Code SEC 8 section 13060. California Food and Agriculture Code, Sacramento, CA.

Burkhard, N., 1978. Hydrolysis of methidathion (Supracide®, Ultracide®) under laboratory conditions. Ciba-Geigy Corp. DPR Vol. 298-088, Rec. No. 52709.

Burnett, T.J. (Pan-Agricultural Laboratories, Inc.), 1992. Methidathion: Nature of the residues in citrus. Ciba-Geigy Corp. DPR Vol. 298-179, Rec. No. 138595.

Cassidy, J.E., N.F. Wood, and K. Lasker, 1969. Desmethyl GS-13005 and other metabolites in the urine of rats fed GS-13005-5-carbonyl-^{14}C. Ciba-Geigy Corp. DPR Vol. 298-120, Rec. No. 92597.

Caris, M. (Health and Welfare Canada), 1992. Methidathion. *In*: Pesticide Residues in Food - 1992: Toxicology Evaluations. Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Expert Group on Pesticide Residues. World Health Organization, Geneva.

CDFA, 1994. California Agriculture Statistical Review 1993. Department of Food and Agriculture, Sacramento, CA. 89 pp.

CFR, 1996. Data Requirements for Registration. Code of Federal Regulations, Title 40, Section 158. U.S. Government Printing Office, Washington, D.C.

CFR, 1998. Methidathion, tolerances for residues. Code of Federal Regulations, Title 40, Section 180.298. U.S. Government Printing Office, Washington, D.C. July 1, 1998.

Chang, J.C.F. and A.G. Richter, 1994. Acute neurotoxicity study with methidathion technical in rats. Ciba-Geigy Corp. DPR Vol. 298-169, Rec. No. 138546.

Chang, J.C.F. and J.A. Walberg, 1991. 1-Year dietary toxicity study with GS-13005 in beagle dogs. Ciba-Geigy Corp. DPR Vol. 298-115, Rec. No. 89667. Also reported in: Chang, J.C.F., J.A. Walberg, and W.R. Campbell, 1992. One-year dietary toxicity study with methidathion in beagle dogs. Fund. Appl. Toxicol. 19: 307-314.

Chen, H.H., J.L. Hsueh, S.R. Sirianni and C.C. Huang, 1981. Induction of sister-chromatid exchanges and cell cycle delay in cultured mammalian cells treated with eight organophosphorus pesticides. Mut. Res. 88: 307-316.

Chopade, H.M. and W.C. Dauterman, 1981. Studies on the *in vitro* metabolism of methidathion by rat and mouse liver. Pest. Biochem. Physiol. 15: 105-119.

Chow, E. And J.C. Turnier, 1995. 90-Day subchronic neurotoxicity study with methidathion technical in rats. Ciba-Geigy Corp. DPR Vol. 298-207, Rec. No. 141663.

Ciba-Geigy, 1975. Residue Report - Methidathion - Safflower Seeds. Ciba-Geigy Corp. DPR Vol. 298-044, Rec. No. 21842.

Ciba-Geigy, 1976. Residues observed in cottonseed from multiple applications. Ciba-Geigy Corp. DPR Vol. 298-051, Rec. No. 21849.

Ciba-Geigy, 1977. Results of tests concerning the amount of residues of methidathion remaining in or on safflower seeds, including a description of the analytical method used. Ciba-Geigy Corp. DPR Vol. 298-047, Rec. No. 21845.

Ciba-Geigy, 1982. Autoradiographic DNA repair test on human fibroblasts - GS 13005. Ciba-Geigy Corp. DPR Vol. 298-089, Rec. No. 53777.

Coulston, F. and L. Golberg (Institute of Experimental Pathology and Toxicology), 1971. Two-year safety evaluation study in rhesus monkeys with GS 13005. Ciba-Geigy Corp. DPR Vol. 298-014, Rec. No. 935999.

Daly, D. (ABC Laboratories, Inc.), 1987. Determination of octanol-water partition coefficient of ^{14}C-methidathion. Ciba-Geigy, Corp. DPR Vol. 298-102, Rec. No. 59677.

Das, Y.T. (Innovative Scientific Services, Inc.), 1990. Photodegradation of [^{14}C]methidathion on soil under artificial sunlight. Ciba-Geigy Corp. DPR Vol 298-172, Rec. No. 138550.

Desi, I., M. Palotas, G. Vetro, I. Csolle, M. Nehez, M. Zimanyi, A. Ferke, E. Huszta and L. Nagymajtenyi, 1986. Biological monitoring and health surveillance of a group of greenhouse pesticide sprayers. Toxicol. Letters 33: 91-105.

Donahue, J. (1996). Revised policy on dermal absorption default for pesticides. Memo No. HSM-96005. Worker Health and Safety Branch, Department of Pesticide Regulation, California Environmental Protection Agency .

Dourson, M., G. Charnley and R. Scheuplein, 2002. Differential sensitivity of children and adults to chemical toxicity. II. Risk and regulation. Regul. Toxicol. Pharmacol. 35: 448-467.

DPR, 1992. Sampling for Pesticide Residues in California Well Water, 1992 Well Inventory Data Base, Cumulative Report 1986-1992. California Environmental Protection Agency, Department of Pesticide Regulation.

DPR, 1993a. Sampling for Pesticide Residues in California Well Water, 1993 Update, Well Inventory Data Base. California Environmental Protection Agency, Department of Pesticide Regulation.

DPR, 1993b. Residues in Fresh Produce - 1992. Pesticide Enforcement Branch, Department of Pesticide Regulation, California Environmental Protection Agency, Sacramento, CA.

DPR, 1994. Sampling for Pesticide Residues in California Well Water, 1994 Update, Well Inventory Data Base. California Environmental Protection Agency, Department of Pesticide Regulation.

DPR, 1995a. Sampling for Pesticide Residues in California Well Water, 1995 Update of the Well Inventory Data Base. California Environmental Protection Agency, Department of Pesticide Regulation.

DPR, 1995b. Residues in Fresh Produce - 1993. Pesticide Enforcement Branch, Department of Pesticide Regulation, California Environmental Protection Agency, Sacramento, CA.

DPR, 1995c. Summary of Pesticide Use Report Data Annual 1993. Department of Pesticide Regulation, California Environmental Protection Agency, Sacramento, CA.

DPR, 1996a. Semiannual Report Summarizing the Reevaluation Status of Pesticide Products During the Period of July 1, 1996 through December 31, 1996. California Environmental Protection Agency, Department of Pesticide Regulation.

DPR, 1996b. 1996 Status Report - Pesticide Contamination Prevention Act. Department of Pesticide Regulation, California Environmental Protection Agency, Sacramento, CA.

DPR, 1996c. Residues in Fresh Produce - 1994. Pesticide Enforcement Branch, Department of Pesticide Regulation, California Environmental Protection Agency, Sacramento, CA.

DPR, 1996d. Summary of Pesticide Use Report Annual 1994. Department of Pesticide Regulation, California Environmental Protection Agency, Sacramento, CA.

DPR, 1996e. Summary of Pesticide Use Report Annual 1995. Department of Pesticide Regulation, California Environmental Protection Agency, Sacramento, CA.

DPR, 1997a. Sampling for Pesticide Residues in California Well Water, 1996 Update of the Well Inventory Data Base. California Environmental Protection Agency, Department of Pesticide Regulation.

DPR, 1997b. Residues in Fresh Produce - 1995. Pesticide Enforcement Branch, Department of Pesticide Regulation, California Environmental Protection Agency, Sacramento, CA.

EDSTAC, 1998. Endocrine Disruptor Screening and Testing Advisory Committee (EDSTAC) - Final Report. August 1998.

El-Dawy, Kh., S.S. Abd El-Meged, M.F. Mahmoud, M.F. Dowidar, and A.A. Hassan, 1995. A biochemical study on the erythrocyte membrane in rats after exposure to some commonly used insecticides. Egypt. J. Biochem. 13(2): 329-337.

Ellenhorn, M.J. and D. G. Barceloux, eds., 1988. Pesticides. In: <u>Medical Toxicology: Diagnosis and Treatment of Human Poisoning</u>, pp. 1069-1108. Elsevier, New York. 1512 pp.

Emrani, J., 1992. Methidathion - Metabolism of [2-^{14}C]-methidathion after multiple oral administration to lactating goats. Ciba-Geigy Corp. DPR Vol. 180, Rec. No. 138604.

FDA (Division of Pharmacology, Food and Administration, Department of Health, Education and Welfare), 1959. Appraisal of the Safety of Chemicals in Foods, Drugs and Cosmetics. The Association of Food and Drug Officials of the United States, Austin, Texas.

Folinusz, P., K. Huber, D.M. Schiavo, J.R. Hazelette, and J.D. Green, 1986. Methidathion - 21-day dermal toxicity study in rabbits (MIN 852128). Ciba-Geigy Corp. DPR Vol. 298-092, Rec. No. 55135.

FPCL (Fisons Pest Control Limited) , 1965a. Effect on reproduction. Ciba-Geigy Corp. DPR Vol. 298-076, Rec. No. 47484.

FPCL (Fisons Pest Control Limited) , 1965b. Neurotoxic effects in the hen. Ciba-Geigy Corp. DPR Vol. 298-076, Rec. No. 935971.

Fritz, H., 1976a. Dominant lethal study on GS 13005 technical - Mouse. Ciba-Geigy Corp. DPR Vol. 298-013, Rec. No. 936073.

Fritz, H., 1976b. Reproduction study GS 13005 tech. - Rat - Seg. II (Test for teratogenic or embryotoxic effects). Ciba-Geigy Corp. DPR Vol. 298-072, Rec. No. 1179.

Fujita, Y., 1985. Studies on contact dermatitis from pesticides in tea growers. Acta Med. Univ. Kagoshima., 27(1): 17-37.

Gaines, T.B. and R.E. Linder, 1986. Acute toxicity of pesticides in adult and weanling rats. Fund. Appl. Toxicol. 7: 299-308.

Ganapathy, C. 1999. Preliminary results of acute and chronic toxicity testing of surface water monitored in the San Joaquin River watershed, winter 1997-1998. Memorandum to Don Weaver, Environmental Monitoring and Pest Management Branch, Department of Pesticide Regulation, California Environmental Protection Agency, Sacramento, CA. January 5, 1999.

Ganapathy, C., C. Nordmark, K. Bennett, A. Bradley, H. Feng, J. Hernandez, and J. White, 1997. Temporal distribution of insecticide residues in four California Rivers. Environmental Hazards Assessment Program, Environmental Monitoring and Pest Management Branch, Department of Pesticide Regulation, California Environmental Protection Agency, Sacramento, CA. Report EH97-06.

Gart, J.J., D. Krewski, P.N. Lee, R.E. Tarone, and J. Wahrendorf, 1986. Statistical Methods in Cancer Research, Vol III - The Design and Analysis of Long-term Animal Experiments. International Agency for Research on Cancer Scientific Publication No. 79. Lyon, France. pp 82-85.

Gaylor, D.W., R.L. Kodell, J.J. Chen, and D. Krewski, 1999. A unified approach to risk assessment for cancer and non-cancer endpoints based on benchmark doses and uncertainty factors. Reg. Toxicol. Pharmacol. 29: 151-157.

Geigy, 1964. Toxicology of GS 13005. Ciba-Geigy Corp. DPR Vol. 298-018, Rec. No. 935972.

Giacobini, E., 2003. Butyrylcholinesterase: Its role in brain function. *In:* Butyrylcholinesterase: It's function and inhibitors (E. Giacobini, ed.). London: Martin Dunitz. pp. 1-19.

Goldenthal, E.I (International Research and Development Corp.), 1986. Methidathion technical - Two-year dietary oncogenicity study in mice. Ciba-Geigy Corp. DPR Vol. 298-079, Rec. No. 45719.

Grisaru, D., M. Sternfeld, A. Eldor, D. Glick, and H. Soreq, 1999. Structural roles of acetylcholinesterase variants in biology and pathology. Eur. J. Biochem., 264: 672-686.

Henderson, J.D., J.T. Yamamoto, D.M. Fry, J.N. Seiber and B.W. Wilson, 1994. Oral and dermal toxicity of organophosphate pesticides in the domestic pigeon (*Columbia livia*). Bull. Environ. Contam. Toxicol. 52: 633-640.

Hertner, T., 1988. Methidathion technical (GS-13005) - Tests for other genotoxic effects - Autoradiographic DNA repair test on rat hepatocytes. Ciba-Geigy Corp. DPR Vol. 298-113, Rec. No. 87195.

Hertner, T., 1990. Methidathion technical (GS-13005) - Tests for other genotoxic effects - Autoradiographic DNA repair test on rat hepatocytes. Ciba-Geigy Corp. DPR Vol. 298-113, Rec. No. 87194.

Holbert, M.S. (Stillmeadow, Inc.), 1989. Supracide 2E - Acute inhalation toxicity study in rats. Ciba-Geigy Corp. DPR Vol. 298-114, Rec. No. 91791.

Holbert, M.S. (Stillmeadow, Inc.), 1992. Supracide 25 WP - Acute inhalation toxicity study in rats. Ciba-Geigy Corp. DPR Vol. 298-132, Rec. No. 116917.

Honeycutt, R.C., 1986a. Field soil dissipation study of Supracide® 2E (methidathion) applied to alfalfa in Fresno County, California. Ciba-Geigy Corp. DPR Vol. 298-088, Rec. No. 52716.

Honeycutt, R.C., 1986b. Field soil dissipation study of Supracide® 2E (methidathion) applied to bareground plots in Vero Beach, Florida. Ciba-Geigy Corp. DPR Vol. 298-088, Rec. No. 52717.

Hool, G., 1980a. Sister chromatid exchange study - GS 13005 - Chinese Hamster. Ciba-Geigy Corp. DPR Vol. 298-003, Rec. No. 936027.

Hool, G., 1980b. Nucleus anomaly test in somatic interphase nuclei of Chinese hamster. Ciba-Geigy Corp. DPR Vol. 298-003, Rec. No. 936021.

Hool, G., 1980c. Nucleus anomaly test in somatic interphase nuclei - GS 12956 - Chinese hamster test for mutagenic effects on bone marrow cells. Ciba-Geigy Corp. DPR Vol. 298-003, Rec. No. 936028.

Hummel, H.E., M.A. Youreneff, M.L.A. Giknis, A.T. Arthur, and E.T. Yau, 1987. Methidathion - a teratology (segment II) study in rabbits. Ciba-Geigy Corp. DPR Vol. 298-096, Rec. No. 55140.

IBT (Industrial Bio-Test Laboratories), 1980. Carcinogenicity evaluation with methidathion technical in albino mice. Ciba-Geigy Corp. DPR Vol. 298-016 & -017, Rec. Nos. 936007 & 936012.

Ito, N., R. Hasegawa, K. Imaida, Y. Kurata, A. Hagiwara and T. Shirai, 1995. Effect of ingestion of 20 pesticides in combination at acceptable daily intake levels on rat liver carcinogenesis. Food Chem. Toxicol. 33(2): 159-163.

JMPR, 1999. Interpretation of cholinesterase inhibition. Pesticide Residues in Food – 1998. Report of the Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Core Assessment Group on Pesticide Residues, Rome, Italy, 21-30 September 1998. FAO Plant Production and Protection Paper 148. Rome: World Health Organization and Food and Agriculture Organization of the United Nations. pp. 17-19.

Johnston, C.D. (Woodard Research Corp.), 1967. GS 13005 - Safety evaluation by two-year feeding studies in rats and dogs. Ciba-Geigy Corp. DPR Vol. 298-010, Rec. No. 935997.

Kahrs, R.A. and M.J. Kanuk, 1969. Determination of residues of GS-13005 in cotton seed and cotton seed fractions by gas chromatography. Ciba-Geigy Corp. DPR Vol. 298-051, Rec. No. 20420.

Kennedy, E.T., 1992. Methidathion - Metabolism of [2-^{14}C]-methidathion in laying hens. Ciba-Geigy Corp. DPR Vol. 298-181, Rec. No. 138612.

Kesterson, a. (PTRL-East, Inc.), 1991. Laboratory volatility of [^{14}C]methidathion. Ciba-Geigy Corp. DPR Vol. 298-176, Rec. No. 138581.

Kieatiwong, S. (PTRL-West, Inc.), 1992. Photodegradation of [^{14}C]methidathion in the vapor phase by natural sunlight. Ciba-Geigy Corp. DPR Vol. 298-174, Rec. No. 138562.

Kishi, M., N. Hirschhorn, M. Djajadosastra, L.N. Satterlee, S. Strowman and R. Ditts, 1995. Relationship of pesticide spraying to signs and symptoms in Indonesian farmers.

Scand. J. Work Environ. Health 21: 124-133.

Kuhn, J.O. (Stillmeadow, Inc.), 1989a. Supracide 2E - Acute oral toxicity study in rats. Ciba-Geigy Corp. DPR Vol. 298-114, Rec. No. 91789.

Kuhn, J.O. (Stillmeadow, Inc.), 1989b. Supracide 2E - Acute dermal toxicity study in rabbits. Ciba-Geigy Corp. DPR Vol. 298-114, Rec. No. 91790.

Kuhn, J.O. (Stillmeadow, Inc.), 1989c. Supracide 2E - Primary dermal irritation study in rabbits. Ciba-Geigy Corp. DPR Vol. 298-114, Rec. No. 91793.

Kuhn, J.O. (Stillmeadow, Inc.), 1989d. Supracide 2E - Primary eye irritation study in rabbits. Ciba-Geigy Corp. DPR Vol. 298-114, Rec. No. 91792.

Kuhn, J.O. (Stillmeadow, Inc.), 1989e. Supracide 2E - Dermal sensitization study in guinea pigs. Ciba-Geigy Corp. DPR Vol. 298-114, Rec. No. 91794.

Kuhn, J.O. (Stillmeadow, Inc.), 1992a. Supracide 25 WP - Acute oral toxicity study in rats. Ciba-Geigy Corp. DPR Vol. 298-132, Rec. No. 116912.

Kuhn, J.O. (Stillmeadow, Inc.), 1992b. Supracide 25 WP - Acute dermal toxicity study in rabbits. Ciba-Geigy Corp. DPR Vol. 298-132, Rec. No. 116915.

Kuhn, J.O. (Stillmeadow, Inc.), 1989c. Supracide 25 WP - Primary dermal irritation study in rabbits. Ciba-Geigy Corp. DPR Vol. 298-132, Rec. No. 116921.

Kuhn, J.O. (Stillmeadow, Inc.), 1989d. Supracide 25 WP - Primary eye irritation study in rabbits. Ciba-Geigy Corp. DPR Vol. 298-132, Rec. No. 116919.

Kuhn, J.O. (Stillmeadow, Inc.), 1989e. Supracide 25 WP - Dermal sensitization study in guinea pigs. Ciba-Geigy Corp. DPR Vol. 298-132, Rec. No. 116922.

Kuhn, J.O. (Stillmeadow, Inc.), 1989f. Acute delayed neurotoxicity of methidathion tech FL 890331 in domestic fowl. Ciba-Geigy Corp. DPR Vol. 298-110, Rec. No. 90269.

Lail, L.J., 1991. Technical methidathion - product chemistry. Ciba-Geigy Corp. DPR Vol. 298-156, Rec. No. 138463.

Leffingwell, T., 1989. Evaluation summary of ground water protection data - methidathion. Department of Pesticide Regulation, California Environmental Protection Agency. DPR Vol. 298-106.

Lefkowitz, R. J., B. B. Hoffman and P. Taylor, 1990. Neurohumoral Transmission: The Autonomic and Somatic Motor Nervous Systems. In: Goodman and Gilman's: The Pharmacological Basis of Therapeutics 8th Edition (Gilman, A.G., T. W. Rall, A. S. Nies and P. Taylor, Eds.), pp. 84-130. Pergamon Press, New York. 1811 pp.

Li, B., J.A. A. Ticu, W. Xie, L.M. Schopfer, P. Hammond, S. Brimijoin, S.H. Hinrichs and O. Lockridge, 2000. Abundant tissue butyrylcholinesterase and its possible function in the acetylcholinesterase knockout mouse. J. Neurochem. 75(3): 1320-1331.

Lippens, R., M. Claeys, C. Waildemauwe, N. Van Larebeke, 1983. Mutagenicity studies on 10 pesticides, on trichloroethane and on diaminobenzidine. Mutat. Res. 113: 277-278.

Lockridge, O. 1990. Genetic variants of human serum cholinesterase influence metabolism of the muscle relaxant succinylcholine. Pharmacol. Ther. 47(1): 35-60.

Lockridge, O. and P. Masson, 2000. Pesticides and susceptible populations: people with butyrylcholinesterase genetic variants may be at risk. Neurotoxicology. 21(1-2): 113-126.

Lodovici, M., S. Aiolli, C. Monserrat, P. Dolara, A. Medica, and P. DiSimplicio, 1994. Effect of a mixture of 15 commonly used pesticides on DNA levels of 8-hydroxy-2-deoxyguanosine and xenobiotic metabolizing enzymes in rat liver. J. Environ. Pathol. Toxicol. Oncol. 13(3): 163-168.

MacCoy, D., K.L. Crepeau, and K.M. Kuivilia, 1995. Dissolved pesticide data for the San Joaquin River at Vernalis and the Sacramento river at Sacramento, California, 1991-1994. U.S. Geological Survey Open-File Report 95-110.

Mainiero, J., E.J. Levy, R.N. Infurna and E.T. Yau, 1987. Methidathion technical - a teratology (Segment II) study in rats. Ciba-Geigy Corp. DPR Vol. 298-095, Rec. No. 55139.

Marcsinsin, J.F., K.V. Wimbert, R.N. Infurna, and E.T. Yau, 1986. Methidathion technical - a dose rangefinding study in pregnant rats. Ciba-Geigy Corp. DPR Vol. 298-094, Rec. No. 55138.

Martinson, J.P. (Springborn Life Sciences, Inc.), 1988. Determination of adsorption and desorption coefficients of methidathion. Ciba-Geigy Corp. DPR Vol. 298-105, Rec. No. 69522.

Matsushita, T. K. Aoyama, K. Yoshimi, Y. Fujita, and A. Ueda, 1985. Allergic contact dermatitis from organophosphate insecticides. Indust. Health 23: 145-153. Also reported in: Matsushita, T. and K. Aoyama, 1981. Cross reactions between some pesticides and the fungicide benomyl in contact allergy. Indust. Health 19: 77-83.

Mattson, A.M., 1975. Methidathion (GS-13005) - Almonds - Results of tests on the amount of residue remaining, including description of the analytical method. Ciba-Geigy Corp. DPR Vol., Rec. No. 20428.

Mionetto, N., R. Rouillon, and J.-L. Marty, 1992. Inhibition of acetylcholinesterase by organophosphorus and carbamates compounds. Studies on free and immobilized enzymes. Z. Wasser-Abwasser-Forsch. 25: 171-174.

Nehéz, M., P. Boros, A. Ferke, J. Mohos, M. Palotás, G. Vetró, M. Zimányi, and I. Dési, 1988. Cytogenetic examination of people working with agrochemicals in the southern region of Hungary. Regul. Toxicol. Pharmacol. 8: 37-44.

Newell, J., 1987. Density of methidathion technical. Ciba-Geigy Corp. DPR Vol. 298-104, Rec. No. 69240.

Nordmark, C. 1997. Preliminary results of acute and chronic toxicity testing of surface water monitored in the Sacramento River watershed, winter 1996-1997. Memorandum to Don Weaver, Environmental Monitoring and Pest Management Branch, Department of Pesticide Regulation, Sacramento, CA. June 6, 1997.

Nordmark, C. 1998. Preliminary results of acute and chronic toxicity testing of surface water monitored in the Sacramento River watershed, winter 1997-1998. Memorandum to Don Weaver, Environmental Monitoring and Pest Management Branch, Department of Pesticide Regulation, Sacramento, CA. July 31, 1998.

Osherhoff, M.R. (Hazleton Laboratories America, Inc.), 1987a. 10-Day dermal dose range finding study in rabbits with methidathion technical. Ciba-Geigy Corp. DPR Vol. 298-092, Rec. No. 55136.

Osherhoff, M.R. (Hazleton Laboratories America, Inc.), 1987b. 21-Day dermal toxicity study in rabbits with methidathion technical. Ciba-Geigy Corp. DPR Vol. 298-093, Rec. No. 55137.

Pantuck, E.J., 1993. Plasma cholinesterase: gene and variations. Anesth. Analg. 77(2): 380-386.

Poletika, N.N. and C.K. Robb, 1998. A monitoring study to characterize chlorpyrifos concentration patterns and ecological risk in an agriculturally dominated tributary of the San Joaquin River. Dow AgroSciencies LLC Study ENV96055. November, 18, 1998.

Powell, S. , 2002. Memorandum: Approximating Confidence Limits for 95th Percentile and Arithmetic Mean Exposures From the Pesticide Handlers Exposure Database (PHED V1.1). Worker Health and Safety Branch, Department of Pesticide Regulation, California Environmental Protection Agency. May 10, 2002.

Quest, J.A. M.P. Copley, K.L. Hamernik, E. Rinde, B. Fisher, R. Engler, W. L. Burnham, and P.A. Fenner-Crisp, 1990. Evaluation of the carcinogenic potential of pesticides. 2. Methidathion. Reg. Toxicol. Pharmacol. 12: 117-126.

Raabe, O.G. (1988). Inhalation uptake of xenobiotic vapors by people. Contract Number CARB A 5-155-33. Air Resources Board, California Environmental Protection Agency.

Radeleff, R.D. and S.E. Kunz, 1972. Toxicity and hazard of diazinon, ethion, and supracide to turkeys. J. Econ. Entomol. 65(1): 162-165.

Raveh, L., E. Grauer, J. Grunwald, E. Cohen, and Y. Ashani, 1997. The stoichiometry of protection against soman and VX toxicity in monkeys pretreated with human butyrylcholinesterase. Toxicol. Appl. Pharmacol. 145:43-53.

Rordorf, B.F., 1988. Report on vapor pressure - methidathion. Ciba-Geigy Corp. DPR Vol. 298-104, Rec. No. 69242.

Ross, L., 1992. Preliminary results of the San Joaquin River study: summer 1991. Memorandum to Kean Goh, Environmental Hazards Assessment Program, Department of Pesticide Regulation, California Environmental Protection Agency, Sacramento, CA. May 21, 1992.

Ross, L., 1993. Preliminary results of the San Joaquin River study: summer 1992. Memorandum to Kean Goh, Environmental Hazards Assessment Program, Department of Pesticide Regulation, California Environmental Protection Agency, Sacramento, CA. September 22, 1993.

Ross, L.J., R. Stein, J. Hsu, J. White, and K. Hefner, 1996. Distribution and mass loading of insecticides in the San Joaquin River, California: winter 1991-92 and 1992-93. Environmental Hazards Assessment Program, Department of Pesticide Regulation, Sacramento, CA. EH 96-02.

Ross, L.J., R. Stein, J. Hsu, J. White, and K. Hefner, 1999. Distribution and mass loading of insecticides in the San Joaquin River, California: spring 1991 and 1992. Environmental Hazards Assessment Program, Environmental Monitoring and Pest Management Branch, Department of Pesticide Regulation, California Environmental Protection Agency, Sacramento, CA. Report EH 99-01.

Salamon, C. (American Biogenics Corp.), 1986. Two-generation reproduction study in albino rats with methidathion technical. Ciba-Geigy Corp. DPR Vol. 298-097, Rec. No. 55142.

Salamon, C. (American Biogenics Corp.), 1987. Methidathion - Two-generation reproduction study in rats. Ciba-Geigy Corp. DPR Vol. 298-098, Rec. No. 55143.

Satou, S., Y. Kimura, K. Yamamoto, and A. Ichihara (Nomura Research Institute), 1979. *In vitro* microbiological assays for mutagenicity testing of DMTP (methidathion). Ciba-Geigy Corp. DPR Vol. 298-003, Rec. No. 936019.

Saxena, A.M. (Hazelton Laboratory America, Inc.), 1989a. Artificial sunlight photodegradation of ^{14}C-methidathion in a buffered aqueous solution. Ciba-Geigy Corp. DPR Vol. 298-171, Rec. No. 138548.

Saxena, A.M. (Hazelton Laboratory America, Inc.), 1989b. Artificial sunlight photodegradation of ^{14}C-methidathion in soil. Ciba-Geigy Corp. DPR Vol. 298-108, Rec. No. 85619.

Saxena, A.M. (Hazelton Laboratories America, Inc.), 1990. Aerobic, aerobic/anaerobic, and sterile soil metabolism of ^{14}C-methidathion. Ciba-Geigy Corp. DPR Vol. 298-111, Rec. No. 90382.

Schlinke, J.C. and J.S. Palmer, 1971. Preliminary toxicologic study of three organophosphate insecticidal compounds in turkeys. 32(3): 495-498.

Silvoy, J.J. (Landis International, Inc.), 1991a. Supracide® 2E field dissipation terrestrial study on citrus in California. Ciba-Geigy Corp. DPR Vol. 298-177, Rec. No. 138583.

Silvoy, J.J. (Landis International, Inc.), 1991b. Supracide® 2E field dissipation terrestrial study on bareground in California. Ciba-Geigy Corp. DPR Vol. 298-178, Rec. No. 138585.

Simmon, V.F. and D. Poole (Stanford Research Institute), 1977. *In vitro* and *in vivo* microbiological assays of six Ciba-Geigy chemicals. Ciba-Geigy Corp. DPR Vol. 298-003, Rec. No. 936020.

Simoneaux, B.J., 1991. Nature of methidathion residues in plants - An overview. Ciba-Geigy Corp. DPR Vol. 298-192, Rec. No. 138631.

Simoneaux, B.J., 1993. ^{14}C-Methidathion: Identification of citrus metabolites. Ciba-Geigy Corp. DPR Vol. 298-190, Rec. No. 138627.

Simoneaux, B. and G.J. Marco, 1984. Dermal absorption of thiadiazole-^{14}C-methidathion by mice. Ciba-Geigy Corp. DPR Vol. 298-107, Rec. No. 87683.

Shepler, K. (PTRL-West, Inc.), 1992. Aged leaching of [^{14}C]methidathion in four soil types. Ciba-Geigy Corp. DPR Vol. 298-175, Rec. No. 138578.

Smith, R.P., 1996. Toxic responses of the blood. *In:* Casarett & Doull's Toxicology: The Basic Science of Poisons, 5th ed. (Klaassen, ed.). McGraw-Hill, New York. pp 335-354.

Strasser, F.F., 1980. Point mutation assay with mouse lymphoma cells - Host mediated assay with GS 13005. Ciba-Geigy Corp. DPR Vol. 298-003, Rec. No. 936017.

Suter, P., 1983. Photolysis of methidathion (Supracide®, Ultracide®) in aqueous medium under laboratory conditions. Ciba-Geigy Corp. DPR Vol. 298-088, Rec. No. 52710

Szolics, I.M., 1987. Disposition of methidathion in the rat (general metabolism). Ciba-Geigy Corp. DPR Vol. 298-128, Rec. No. 92634.

TAS, 1996a. Exposure 4™, Detailed Distributional Dietary Exposure Analysis, Version 3.35. Technical Assessment Systems, Inc., Washington, D.C.

TAS, 1996b. Exposure 1™, Chronic Dietary Exposure Analysis, Version 3.35. Technical Assessment Systems, Inc., Washington, D.C.

Teitelman, U., M. Alder and I. Levy, 1975. Treatment of massive poisoning by the organophosphate pesticide methidathion. Clin. Toxicol. 8(3): 277-282.

Tong, C., 1982a. The hepatocyte primary culture/DNA repair assay on compound GS-13005-008266 using mouse hepatocytes in culture. Ciba-Geigy Corp. DPR Vol. 298-089, Rec. No. 53774.

Tong, C., 1982b. The hepatocyte primary culture/DNA repair assay on compound GS-13005-008266 using rat hepatocytes in culture. Ciba-Geigy Corp. DPR Vol. 298-089, Rec. No. 53775.

Travaglini, R., 1999. Human Health Risk Assessment - Methidathion. U.S. Environmental Protection Agency, Office of Pesticide Programs, Health Effects Division (7509C). December 8, 1999.

Tsatsakis, A.M., P. Aguridakis, M.N. Michalodimitrakis, A.K. Tsakalov, A.K. Alegakis, E.

Koumantakis and G. Troulakis, 1996. Experiences with acute organophosphate poisonings in Crete. Vet. Human Toxicol. 38(2): 101-107.

Ullman, L., no date. Neurotoxicity study in domestic fowls, 42 days. Ciba-Geigy Corp. DPR Vol. 298-012, Rec. No. 935981.

USDA, 1989-91. Food and Nutrient Intake by Individuals in the United States, 1 Day, 1989-1992. Continuing Survey of Food Intakes by Individuals, 1989-1992.. Agricultural Research Service, U.S. Department of Agriculture.

USDA, 1992. Agricultural Chemical Usage 1991 Fruits Summary. National Agricultural Statistics Service, U.S. Department of Agriculture, Washington, D.C. 120 pp.

USDA, 1994a. Agricultural Chemical Usage 1993 Fruits Summary. National Agricultural Statistics Service, U.S. Department of Agriculture, Washington, D.C. 146 pp.

USDA, 1994b. Agricultural Statistics 1994. National Agricultural Statistics Service, U.S. Department of Agriculture, Washington, D.C. 485 pp.

USDA, 1996a. Agricultural Chemical Usage 1995 Fruits Summary. National Agricultural Statistics Service, U.S. Department of Agriculture, Washington, D.C. 119 pp.

USDA, 1996b. Pesticide Data Program (PDP) Annual Summary Calendar Year 1994 (Franks, W.I. and R.L. Epstein, eds.). Agricultural Marketing Service, U.S. Department of Agriculture, Washington, D.C. 105 pp.

USDA, 1997. Pesticide Data Program (PDP) Annual Summary Calendar Year 1995 (Figueroa, E.E. and R.L. Epstein, eds.). Agricultural Marketing Service, U.S. Department of Agriculture, Washington, D.C. 68 pp.

USDA, 1998a. Pesticide Data Program (PDP) Annual Summary Calendar Year 1996 (Figueroa, E.E. and R.L. Epstein, eds.). Agricultural Marketing Service, U.S. Department of Agriculture, Washington, D.C. 63 pp.

USDA, 1998b. Pesticide Data Program (PDP) Annual Summary Calendar Year 1997 (Figueroa, E.E. and R.L. Epstein, eds.). Agricultural Marketing Service, U.S. Department of Agriculture, Washington, D.C. 100 pp.

U.S. EPA, 1982. Pesticide Assessment Guidelines Subdivision O- Residue Chemistry. Office of Pesticides and Toxic Substances document # EPA-540/9-82-023.

U.S. EPA, 1989. Guidance for the Reregistration of Pesticide Products Containing Methidathion. Office of Pesticide Programs, U.S. Environmental Protection Agency, Washington, D.C.

U.S. EPA, 1991. For Your Information- Pesticide Tolerances. Pesticide and Toxic Substances (H7506C), August, 1991.

U.S. EPA, 1992. Draft report: A cross-species scaling factor for carcinogen risk assessment based on equivalence of mg/kg$^{3/4}$/day; Notice. Federal Register 57(109): 24152-24173.

U.S. EPA, 1993. An SAB Report: Cholinesterase Inhibition and Risk Assessment. Review of the Risk Assessment Forum's Draft *Guidance on the Use of Data on Cholinesterase Inhibition in Risk Assessment by the SAB/SAP Joint Committee.* U.S. Environmental Protection Agency. EPA-SAB-EHC-93-011.

U.S. EPA, 1994. Pesticide Assessment Guidelines, Subdivision O, Residue Chemistry, Table II Update (June 1994), Raw Agricultural and Processed Commodities and Livestock Feeds Derived from Field Crops. U.S. Environmental Protection Agency.

U.S. EPA, 1997a. The Federal Insecticide Fungicide, and Rodenticide Act (FIFRA) and Federal Food, Drug, and Cosmetic Act (FFDCA) as Amended by the Food Quality Protection Act (FQPA) of August 3, 1996. Document no. 730L97001, March 1997. Office of Pesticide Programs, U.S. Environmental Protection Agency, Washington, D.C.

U.S. EPA, 1997b. 1996 Food Quality Protection Act Implementation Plan. March, 1977. Office of Prevention, Pesticides and Toxic Substances (7506C), U.S. Environmental Protection Agency, Washington, D.C. (http://www.epa.gov/fedrgstr/)

U.S. EPA, 1997c. Special Report on Environmental Endocrine Disruption: An Effects Assessment and Analysis. Risk Assessment Forum, U.S. Environmental Protection Agency, Washington, D.C.

U.S. EPA, 1997d. Raw and Processed Food Schedule for Pesticide Tolerance Reassessment. Federal Register 62(149): 42020-42030.

U.S. EPA, 1998. Memorandum - Methidathion. Chem No. 100301. Acute Dietary Risk Assessment (Monte Carlo analysis) DP Barcode D243700. Health Effects Division, Office of Pesticide Programs, U.S. Environmental Protection Agency. October 16, 1998.

U.S. EPA, 1999. Drinking Water Regulations and Health Advisories. Office of Water, U.S. Environmental Protection Agency. Website: http://www.eoa.gov/oswater/Tools/ dwstds0.html.

U.S. EPA, 2000a. Office of Pesticide Programs Science Policy on the Use of Data on Cholinesterase Inhibition for Risk Assessments of Organophosphorus and Carbamate Pesticides. Office of Pesticide Programs, U.S. Environmental Protection Agency, Washington, D.C. August 18, 2000.

U.S. EPA, 2000b. Fenthion, Methidathion, Naled, Phorate and Profenofos; Proposed Revocation of Tolerances. Federal Register 65(63): 17236-17239.

U.S. EPA, 2001. Preliminary Cumulative Risk assessment of the Organophosphorus Pesticides. Office of Pesticide Programs, U.S. Environmental Protection Agency. December 3, 2001. (http://www.epa.gov/pesticides/cumulative/pra-op)

U.S. EPA, 2002a. Interim Reregistration Eligibility Decision for Methidathion. Office of Prevention, Pesticides and Toxic Substances, U.S. Environmental Protection Agency. April 9, 2002 (http://www.epa.gov/oppsrrd1/REDs/methidathion_ired.pdf)

U.S. EPA, 2002b. Guidance on Cumulative Risk Assessment of Pesticide Chemicals That Have a Common Mechanism of Toxicity. Office of Pesticide Programs, U.S. Environmental Protection Agency. January 14, 2002. (http://www.epa.gov/pesticides/trac/science/cumulative_guidance.pdf)

U.S. EPA, 2002c. Consideration of the FQPA Safety Factor and Other Uncertainty Factors in Cumulative Risk Assessment of Chemicals Sharing a Common Mechanism of Toxicity. Draft Document. Office of Pesticide Programs, U.S. Environmental Protection Agency. February 28, 2002. (http://www.epa.gov/pesticides/trac/science/consid_draft.pdf)

U.S. EPA, 2005. Guidelines for Carcinogen Risk Assessment. Risk Assessment Forum, U.S. Environmental Protection Agency, Washington, D.C. EPA/630/P-03/001F. March 2005.

U.S. Geological Survey, in preparation. Pesticide monitoring in the Sacramento River Basin for the National Water-Quality Assessment Program, 2/96-9-98.

Wallace, P., 1986. Rabbit - Segment II - Dose range-finding teratology study pilot (P-2). Ciba-Geigy Corp. DPR Vol. 298-096, Rec. No. 55141.

Woodard Research, 1965. Demyelination study in the chicken. Ciba-Geigy Corp. DPR Vol. 298-076, Rec. No. 14846.

Woodard Research, 1966a. GS-13005, 25W - Potentiation studies with other organophosphates in the rat. DPR Vol. 298-018, Rec. No. 936037.

Woodard Research, 1966b. GS-13005, 40W - Three-generation reproduction study in the rat. Ciba-Geigy Corp. DPR Vol. 298-018, Rec. No. 33539.

Wyler, H., 1987. Report on water solubility - methidathion. Ciba-Geigy Corp. DPR Vol. 298-102, Rec. No. 59675.

Yau, E.T., D.N. McMartin, I.H. Zaidi, and J.D. Green, 1986. Methidathion - 2-Year oral oncogenicity and toxicity study in albino rats. Ciba-Geigy Corp. DPR Vol. 298-090, Rec. No. 53935.

Zoppellari, R., L. Targa, P. Tonini and R. Zatelli, 1990. Acute poisoning with methidathion: a case. Human Exper. Toxicol. 9: 415-419.

APPENDICES

Appendix A - Oncogenicity Computer Model Printout

Appendix B - Dietary and Drinking Water Exposure Analysis Printouts

APPENDIX A

Oncogenicity Computer Model Printout

DATE: 06-22-00 TIME: 09:18:12

MULTI-WEIB (MAR 1985)

K.S. CRUMP & COMPANY, INC.
1201 GAINES STREET
RUSTON, LA 71270
(318) 255-4800

Methidathion, Combined Hepatocellular Adenomas and Carcinomas in Male Mice

THE 20 OBSERVATIONS AT LEVEL 1 WITH A DOSE OF .000000

TIME	# OF ANIMALS	TUMOR INDICATOR	TIME	# OF ANIMALS	TUMOR INDICATOR
57.0	1	1	58.0	1	1
59.0	1	1	62.0	1	1
64.0	1	1	67.0	1	1
73.0	2	1	76.0	1	1
77.0	1	1	78.0	1	1
81.0	1	1	81.0	1	3
83.0	2	1	84.0	1	3
93.0	1	1	95.0	1	1
98.0	3	1	99.0	1	3
100.0	22	1	100.0	6	2

THE 20 OBSERVATIONS AT LEVEL 2 WITH A DOSE OF .600000E-01

TIME	# OF ANIMALS	TUMOR INDICATOR	TIME	# OF ANIMALS	TUMOR INDICATOR
44.0	2	1	48.0	1	1
60.0	1	1	61.0	1	1
64.0	1	1	66.0	1	1
77.0	1	1	79.0	1	2
80.0	1	2	81.0	1	1
89.0	1	2	90.0	1	2
91.0	1	2	91.0	1	1
94.0	1	1	96.0	1	1

98.0	3	1	99.0	1	1
100.0	19	1	100.0	10	2

THE 19 OBSERVATIONS AT LEVEL 3 WITH A DOSE OF .200000

TIME	# OF ANIMALS	TUMOR INDICATOR	TIME	# OF ANIMALS	TUMOR INDICATOR
5.0	1	1	12.0	1	1
25.0	1	1	67.0	2	1
71.0	2	1	76.0	1	1
85.0	1	2	89.0	3	1
90.0	1	1	93.0	2	1
93.0	1	2	94.0	1	3
96.0	1	1	96.0	1	3
97.0	1	1	98.0	1	1
99.0	3	1	100.0	19	1
100.0	7	2			

THE 21 OBSERVATIONS AT LEVEL 4 WITH A DOSE OF .970000

TIME	# OF ANIMALS	TUMOR INDICATOR	TIME	# OF ANIMALS	TUMOR INDICATOR
44.0	1	1	57.0	1	1
58.0	2	1	59.0	1	1
60.0	2	1	71.0	1	2
75.0	1	1	79.0	1	1
81.0	1	3	81.0	1	2
83.0	1	2	86.0	1	3
86.0	1	1	87.0	1	2
88.0	1	1	90.0	1	1
91.0	1	3	99.0	1	1
99.0	2	3	100.0	16	1
100.0	12	2			

THE 32 OBSERVATIONS AT LEVEL 5 WITH A DOSE OF 1.90000

TIME	# OF ANIMALS	TUMOR INDICATOR	TIME	# OF ANIMALS	TUMOR INDICATOR
22.0	1	1	28.0	1	1
55.0	1	1	56.0	1	1
57.0	1	1	63.0	1	2
68.0	1	2	69.0	1	1
70.0	1	1	72.0	3	2
74.0	1	2	76.0	1	2

78.0	1	3	80.0	1	2
82.0	1	2	85.0	2	2
88.0	1	3	90.0	3	3
91.0	1	2	91.0	1	3
92.0	1	3	93.0	1	3
93.0	1	2	94.0	1	3
95.0	1	3	98.0	2	1
98.0	1	2	98.0	1	3
99.0	2	2	99.0	2	3
100.0	3	1	100.0	9	2

```
     FORM OF PROBABILITY FUNCTION:
          P(DOSE) = 1 - exp( ( -Q0 - Q1 * D - Q2 * D^2 - ... - Q 4 * D^ 4 ) *
(T - T0)^J )


     THE MAXIMUM LIKELIHOOD ESTIMATION OF:

                         PROBABILITY FUNCTION COEFFICIENTS

                             Q( 0)= .476305436831E-12
                             Q( 1)= .864812104460E-13
                             Q( 2)= .375761739529E-12
                             Q( 3)= .104589214976E-12
                             Q( 4)= .000000000000


                            TIME FUNCTION COEFFICIENTS

                               T0 =  .000000000000
                                J =  5.93342862928


     THE MAXIMUM LIKELIHOOD IS -112.496010523


                     MAXIMUM LIKELIHOOD ESTIMATES OF EXTRA RISK
*******************************************************************************



                WEIBULL LOWER CONFIDENCE LIMITS ON DOSE FOR FIXED RISK
                ******************************************************


                                                            CONFIDENCE
                               LOWER BOUND   UPPER BOUND      LIMIT
     RISK        MLE DOSE        ON DOSE       ON RISK      INTERVAL       TIME
```

----	--------	-------	-------	--------	----
1.000000E-06	1.571056E-05	1.691143E-06	9.289864E-06	95.0%	100.000

WEIBULL UPPER CONFIDENCE LIMITS ON RISK FOR FIXED DOSE
****

DOSE	MLE RISK	UPPER BOUND ON RISK	CONFIDENCE LIMIT INTERVAL	TIME
----	--------	-------	--------	----
1.00000	.341090	.529102	95.0%	100.000

NORMAL COMPLETION!

APPENDIX B

Dietary and Drinking Water Exposure Analysis Printouts

ACUTE EXPOSURE (EX4) ANALYSIS FOR METHIDATHION
Residue file name: METHIAT1 Analysis date: 06-14-2000
1989-92 DATA Adjustment factor #2 NOT used
DPR NOEL (Acute) = 0.300000 mg/kg body-wt/day
COMMENT 1: Tier 1 Analysis - DPR monitoring data + field trial data

RESIDUE FILE LISTING

TAS CODE	CROP GRP	FOOD NAME	RESIDUE (PPM)	ADJ. FCTRS #1	#2	SOURCE CODE
20	K	CITRUS CITRON	no consumption in survey			
22	K	GRAPEFRUIT-PEELED FRUIT	0.128000	0.10	1.00	DPR95%
23	K	GRAPEFRUIT-JUICE	0.128000	0.10	1.00	DPR95%
24	K	KUMQUATS	no consumption in survey			
26	K	LEMONS-PEELED FRUIT	0.057000	0.10	1.00	DPR95%
27	K	LEMONS-PEEL	0.057000	2.50	1.00	DPR95%
28	K	LEMONS-JUICE	0.057000	0.10	1.00	DPR95%
30	K	LIMES-PEELED FRUIT	0.026000	0.10	1.00	DPR95%
31	K	LIMES-PEEL	0.026000	2.50	1.00	DPR95%
32	K	LIMES-JUICE	0.026000	0.10	1.00	DPR95%
33	K	ORANGES-JUICE-CONCENTRATE	0.564000	0.37	1.00	DPR95%
34	K	ORANGES-PEELED FRUIT	0.564000	0.10	1.00	DPR95%
35	K	ORANGES-PEEL	0.564000	2.50	1.00	DPR95%
36	K	ORANGES-JUICE	0.564000	0.10	1.00	DPR95%
37	K	TANGELOS	no consumption in survey			
38	K	TANGERINES	1.030000	0.10	1.00	DPR
39	K	TANGERINES-JUICE	1.030000	0.10	1.00	DPR
40	R	ALMONDS	0.050000	1.00	1.00	TOLERA
41	R	BRAZIL NUTS	0.050000	1.00	1.00	TOLERA
42	R	CASHEWS	0.050000	1.00	1.00	TOLERA
43	R	CHESTNUTS	0.050000	1.00	1.00	TOLERA
44	R	FILBERTS (HAZELNUTS)	0.050000	1.00	1.00	TOLERA
45	R	HICKORY NUTS	0.050000	1.00	1.00	TOLERA
46	R	MACADAMIA NUTS (BUSH NUTS)	0.050000	1.00	1.00	TOLERA
47	R	PECANS	0.050000	1.00	1.00	TOLERA
48	R	WALNUTS	0.050000	1.00	1.00	TOLERA
49	R	BUTTER NUTS	no consumption in survey			
50	A	PISTACHIO NUTS	0.050000	1.00	1.00	TOLERA
51	R	BEECHNUTS	no consumption in survey			
52	L	APPLES	0.010000	1.00	1.00	DPR
53	L	APPLES-DRIED	0.010000	8.00	1.00	DPR
54	L	APPLES-JUICE/CIDER	0.010000	1.30	1.00	DPR
55	L	CRABAPPLES	no consumption in survey			
56	L	PEARS	0.012000	1.00	1.00	DPR95%
57	L	PEARS-DRIED	0.012000	6.25	1.00	DPR95%
58	L	QUINCES	no consumption in survey			

TAS CODE	CROP GRP	FOOD NAME	RESIDUE (PPM)	ADJ. FCTRS #1	#2	SOURCE CODE
59	M	APRICOTS	0.010000	1.00	1.00	DPR
60	M	APRICOTS-DRIED	0.010000	6.00	1.00	DPR
61	M	CHERRIES	0.010000	1.00	1.00	DPR
62	M	CHERRIES-DRIED	no consumption in survey			
63	M	CHERRIES-JUICE	0.010000	1.50	1.00	DPR
64	M	NECTARINES	0.010000	1.00	1.00	DPR
65	M	PEACHES	0.010000	1.00	1.00	DPR
66	M	PEACHES-DRIED	0.010000	7.00	1.00	DPR
67	M	PLUMS(DAMSONS)	0.010000	1.00	1.00	DPR
68	M	PLUMS-PRUNES(DRIED)	0.010000	5.00	1.00	DPR
69	M	PLUMS/PRUNE-JUICE	0.010000	1.40	1.00	DPR
80	A	MANGOES	0.050000	1.00	1.00	TOLERA
82	A	OLIVES	0.050000	1.00	1.00	TOLERA
97	A	KIWI FRUIT	0.010000	1.00	1.00	DPR
103	A	SUGAR APPLES (SWEETSOP)	no consumption in survey			
106	A	CARAMBOLA (STARFRUIT)	no consumption in survey			
108	A	LONGAN FRUIT	no consumption in survey			
181	A	ARTICHOKES-GLOBE	0.040000	1.00	1.00	DPR
203	B	ARTICHOKES-JERUSALEM	no consumption in survey			
246	A	SUNFLOWER-SEEDS-WITH HULLS	no consumption in survey			
275	O	SORGHUM (INCLUDING MILO)	no consumption in survey			
290	A	COTTONSEED-OIL	0.200000	1.00	1.00	TOLERA
291	A	COTTONSEED-MEAL	0.200000	1.00	1.00	TOLERA
294	A	SAFFLOWER-SEED	no consumption in survey			
295	A	SAFFLOWER-OIL	0.500000	1.00	1.00	TOLERA
298	A	SUNFLOWER-OIL	0.500000	1.00	1.00	TOLERA
300	A	OLIVE OIL	0.050000	1.00	1.00	TOLERA
318	X	MILK-NONFAT SOLIDS	0.000350	7.87	1.00	REGIST
319	X	MILK-FAT SOLIDS	0.000350	7.87	1.00	REGIST
320	X	MILK SUGAR (LACTOSE)	0.000350	8.13	1.00	REGIST
321	U	BEEF-MEAT BYPRODUCTS	0.000920	1.00	1.00	REGIST
322	U	BEEF(ORGAN MEATS)-OTHER	0.000920	1.00	1.00	REGIST
323	U	BEEF-DRIED	0.000920	1.92	1.00	REGIST
324	U	BEEF(BONELESS)-FAT	0.000100	1.00	1.00	REGIST
325	U	BEEF(ORGAN MEATS)-KIDNEY	0.000600	1.00	1.00	REGIST
326	U	BEEF(ORGAN MEATS)-LIVER	0.000920	1.00	1.00	REGIST
327	U	BEEF(BONELESS)-LEAN (FAT/FREE)	0.000920	1.00	1.00	REGIST
328	U	GOAT-MEAT BYPRODUCTS	no consumption in survey			
329	U	GOAT(ORGAN MEATS)-OTHER	0.000920	1.00	1.00	REGIST
330	U	GOAT(BONELESS)-FAT	no consumption in survey			
331	U	GOAT(ORGAN MEATS)-KIDNEY	no consumption in survey			
332	U	GOAT(ORGAN MEATS)-LIVER	no consumption in survey			
333	U	GOAT(BONELESS)-LEAN (FAT/FREE)	no consumption in survey			
334	U	HORSE	no consumption in survey			
336	U	SHEEP-MEAT BYPRODUCTS	no consumption in survey			
337	U	SHEEP(ORGAN MEATS)-OTHER	no consumption in survey			

TAS CODE	CROP GRP	FOOD NAME	RESIDUE (PPM)	ADJ. FCTRS #1	#2	SOURCE CODE
338	U	SHEEP(BONELESS)-FAT	0.000100	1.00	1.00	REGIST
339	U	SHEEP(ORGAN MEATS)-KIDNEY	no consumption in survey			
340	U	SHEEP(ORGAN MEATS)-LIVER	no consumption in survey			
341	U	SHEEP(BONELESS)-LEAN (FAT FREE	0.000920	1.00	1.00	REGIST
342	U	PORK-MEAT BYPRODUCTS	0.000440	1.00	1.00	REGIST
343	U	PORK(ORGAN MEATS)-OTHER	no consumption in survey			
344	U	PORK(BONELESS)-FAT	0.000050	1.00	1.00	REGIST
345	U	PORK(ORGAN MEATS)-KIDNEY	no consumption in survey			
346	U	PORK(ORGAN MEATS)-LIVER	0.000440	1.00	1.00	REGIST
347	U	PORK(BONELESS)-LEAN (FAT FREE)	0.000440	1.00	1.00	REGIST
355	V	TURKEY-BYPRODUCTS	0.000210	1.00	1.00	REGIST
356	V	TURKEY-GIBLETS (LIVER)	0.000210	1.00	1.00	REGIST
357	V	TURKEY-(BONELESS)-FAT	0.000070	1.00	1.00	REGIST
358	V	TURKEY-(BONELESS)LEAN/FAT FREE	0.000110	1.00	1.00	REGIST
359	V	TURKEY-UNSPECIFIED	no consumption in survey			
360	V	POULTRY-OTHER-LEAN (FAT FREE)	0.000110	1.00	1.00	REGIST
361	V	POULTRY-OTHER-GIBLETS(LIVER)	no consumption in survey			
362	V	POULTRY-OTHER-FAT	0.000070	1.00	1.00	REGIST
363	X	EGGS-WHOLE	0.000130	1.00	1.00	REGIST
364	X	EGGS-WHITE ONLY	0.000130	1.00	1.00	REGIST
365	X	EGGS-YOLK ONLY	0.000130	1.00	1.00	REGIST
366	V	CHICKEN-BYPRODUCTS	no consumption in survey			
367	V	CHICKEN-GIBLETS(LIVER)	0.000210	1.00	1.00	REGIST
368	V	CHICKEN (BONELESS)-FAT	0.000070	1.00	1.00	REGIST
369	V	CHICKEN(BONELESS)LEAN/FAT FREE	0.000110	1.00	1.00	REGIST
377	L	APPLES-JUICE-CONCENTRATE	0.010000	3.90	1.00	DPR
385	V	CHICKEN-GIBLETS (EXCL. LIVER)	0.000210	1.00	1.00	REGIST
398	X	MILK-BASED WATER	0.000350	1.00	1.00	REGIST
402	M	PEACHES-JUICE	0.010000	1.00	1.00	DPR
404	L	PEARS-NECTAR	0.012000	1.00	1.00	DPR95%
410	M	APRICOT JUICE OR NECTAR	0.010000	1.00	1.00	DPR
417	A	SUNFLOWER-SEEDS-HULLED	0.500000	1.00	1.00	TOLERA
420	K	TANGERINES-JUICE-CONCENTRATE	no consumption in survey			
424	U	VEAL-(BONELESS)-FAT	0.000100	1.00	1.00	REGIST
425	U	VEAL-(BONELESS)-LEAN (FAT FREE	0.000920	1.00	1.00	REGIST
426	U	VEAL-(ORGAN MEATS)-KIDNEY	no consumption in survey			
427	U	VEAL-(ORGAN MEATS)-LIVER	no consumption in survey			
428	U	VEAL-(ORGAN MEATS)-OTHER	no consumption in survey			
429	U	VEAL-DRIED	no consumption in survey			
430	U	VEAL-MEAT BYPRODUCTS	no consumption in survey			
431	R	WALNUT OIL	no consumption in survey			
441	K	GRAPEFRUIT-JUICE-CONCENTRATE	0.128000	0.39	1.00	DPR
442	K	LEMONS-JUICE-CONCENTRATE	0.057000	0.57	1.00	DPR
443	K	LIMES-JUICE-CONCENTRATE	0.026000	0.30	1.00	DPR
448	K	GRAPEFRUIT PEEL	no consumption in survey			
449	V	TURKEY-(ORGAN MEATS)-OTHER	0.000210	1.00	1.00	REGIST

ACUTE EXPOSURE (EX4) ANALYSIS FOR METHIDATHION
Residue file name: METHIAT1 Analysis date: 06-14-2000
1989-92 DATA Adjustment factor #2 NOT used
DPR NOEL (Acute) = 0.300000 mg/kg body-wt/day
Initial estimate of user-days as % of person-days in survey = 100.00%
COMMENT 1: Tier 1 Analysis - DPR monitoring data + field trial data

U.S. POP - ALL SEASONS

Daily Exposure Analysis 1/ (mg/kg body-weight/day)

	per Capita	per User
Mean	0.000102	0.000103
Standard Deviation	0.000189	0.000190
Standard Error	0.000001	0.000001

Percent of Person-Days that are User-Days = 99.47%

ESTIMATED PERCENTILE OF USER-DAYS LESS THAN/EQUAL TO CALCULATED EXPOSURE
in mg/kg body-wt/day and corresponding Margin of Exposure (MOE)

PERCENTILE	EXPOSURE	MOE 2/	PERCENTILE	EXPOSURE	MOE
10.00	0.000004	76,508	90.00	0.000270	1,110
20.00	0.000007	40,639	95.00	0.000418	718
30.00	0.000012	24,467	97.50	0.000603	498
40.00	0.000020	15,098	99.00	0.000904	332
50.00	0.000031	9,788	99.50	0.001166	257
60.00	0.000049	6,156	99.75	0.001413	212
70.00	0.000091	3,288	99.90	0.001847	162
80.00	0.000163	1,846			

ESTIMATED PERCENTILE OF PER-CAPITA DAYS LESS THAN/EQUAL TO CALCULATED EXPOSURE
in mg/kg body-wt/day and corresponding Margin of Exposure (MOE)

PERCENTILE	EXPOSURE	MOE 2/	PERCENTILE	EXPOSURE	MOE
10.00	0.000004	80,391	90.00	0.000270	1,112
20.00	0.000007	41,473	95.00	0.000417	719
30.00	0.000012	24,839	97.50	0.000602	498
40.00	0.000020	15,286	99.00	0.000903	332
50.00	0.000030	9,881	99.50	0.001165	258
60.00	0.000048	6,206	99.75	0.001411	213
70.00	0.000091	3,313	99.90	0.001846	163
80.00	0.000162	1,855			

1/ Analysis based on all participant-days in NFCS 1989-92 survey.
2/ Margin of Exposure = NOEL/ Dietary Exposure.

ACUTE EXPOSURE (EX4) ANALYSIS FOR METHIDATHION
Residue file name: METHIAT1 Analysis date: 06-14-2000
1989-92 DATA Adjustment factor #2 NOT used
DPR NOEL (Acute) = 0.300000 mg/kg body-wt/day

WESTERN REGION

	Daily Exposure Analysis (mg/kg body-weight/day) per Capita	per User
Mean	0.000113	0.000114
Standard Deviation	0.000207	0.000208
Standard Error	0.000002	0.000002

Percent of Person-Days that are User-Days = 98.79%

ESTIMATED PERCENTILE OF USER-DAYS LESS THAN/EQUAL TO CALCULATED EXPOSURE
in mg/kg body-wt/day and corresponding Margin of Exposure (MOE)

PERCENTILE	EXPOSURE	MOE 2/	PERCENTILE	EXPOSURE	MOE
10.00	0.000004	74,634	90.00	0.000290	1,034
20.00	0.000007	40,239	95.00	0.000463	647
30.00	0.000013	22,788	97.50	0.000697	430
40.00	0.000022	13,719	99.00	0.001066	281
50.00	0.000034	8,834	99.50	0.001392	216
60.00	0.000054	5,548	99.75	0.001705	176
70.00	0.000105	2,858	99.90	0.001918	156
80.00	0.000177	1,695			

ESTIMATED PERCENTILE OF PER-CAPITA DAYS LESS THAN/EQUAL TO CALCULATED EXPOSURE
in mg/kg body-wt/day and corresponding Margin of Exposure (MOE)

PERCENTILE	EXPOSURE	MOE 2/	PERCENTILE	EXPOSURE	MOE
10.00	0.000004	83,840	90.00	0.000289	1,039
20.00	0.000007	42,134	95.00	0.000461	650
30.00	0.000013	23,665	97.50	0.000694	432
40.00	0.000021	14,131	99.00	0.001063	282
50.00	0.000033	9,030	99.50	0.001388	216
60.00	0.000053	5,650	99.75	0.001701	176
70.00	0.000103	2,910	99.90	0.001916	157
80.00	0.000175	1,712			

ACUTE EXPOSURE (EX4) ANALYSIS FOR METHIDATHION
Residue file name: METHIAT1 Analysis date: 06-14-2000
1989-92 DATA Adjustment factor #2 NOT used
DPR NOEL (Acute) = 0.300000 mg/kg body-wt/day

NURSING INFANTS (<1 YEAR)

	Daily Exposure Analysis (mg/kg body-weight/day) per Capita	per User
Mean	0.000118	0.000339
Standard Deviation	0.000708	0.001169
Standard Error	0.000057	0.000138

Percent of Person-Days that are User-Days = 34.83%

ESTIMATED PERCENTILE OF USER-DAYS LESS THAN/EQUAL TO CALCULATED EXPOSURE in mg/kg body-wt/day and corresponding Margin of Exposure (MOE)

PERCENTILE	EXPOSURE	MOE 2/	PERCENTILE	EXPOSURE	MOE
10.00	0.000008	35,767	90.00	0.000787	381
20.00	0.000028	10,877	95.00	0.001068	281
30.00	0.000032	9,487	97.50	0.001556	193
40.00	0.000036	8,343	99.00	0.004529	66
50.00	0.000050	5,944	99.50	0.007268	41
60.00	0.000121	2,470	99.75	0.008637	35
70.00	0.000176	1,708	99.90	0.009459	32
80.00	0.000198	1,516			

ESTIMATED PERCENTILE OF PER-CAPITA DAYS LESS THAN/EQUAL TO CALCULATED EXPOSURE in mg/kg body-wt/day and corresponding Margin of Exposure (MOE)

PERCENTILE	EXPOSURE	MOE 2/	PERCENTILE	EXPOSURE	MOE
10.00	0.000000	>1,000,000	90.00	0.000178	1,681
20.00	0.000000	>1,000,000	95.00	0.000530	566
30.00	0.000000	>1,000,000	97.50	0.000946	317
40.00	0.000000	>1,000,000	99.00	0.001484	202
50.00	0.000000	>1,000,000	99.50	0.003665	82
60.00	0.000000	>1,000,000	99.75	0.006075	49
70.00	0.000016	18,985	99.90	0.008434	36
80.00	0.000040	7,557			

```
ACUTE EXPOSURE (EX4) ANALYSIS FOR METHIDATHION
Residue file name: METHIAT1                           Analysis date: 06-14-2000
1989-92 DATA   Adjustment factor #2 NOT used
DPR NOEL (Acute) =   0.300000 mg/kg body-wt/day
===============================================================================

NON-NURSING INFANTS (<1)           Daily Exposure Analysis
------------------------           (mg/kg body-weight/day)
                                   per Capita     per User
                                   ----------    ---------
            Mean                      0.000209     0.000218
            Standard Deviation        0.000276     0.000279
            Standard Error            0.000013     0.000013

    Percent of Person-Days that are User-Days = 96.06%


  ESTIMATED PERCENTILE OF USER-DAYS LESS THAN/EQUAL TO CALCULATED EXPOSURE
     in mg/kg body-wt/day and corresponding Margin of Exposure (MOE)

 PERCENTILE    EXPOSURE    MOE 2/         PERCENTILE    EXPOSURE    MOE
 ----------  ----------  ---------        ----------  ----------  ---------
    10.00      0.000035      8,580           90.00      0.000538        557
    20.00      0.000039      7,631           95.00      0.000850        353
    30.00      0.000045      6,693           97.50      0.001041        288
    40.00      0.000054      5,604           99.00      0.001276        235
    50.00      0.000104      2,874           99.50      0.001703        176
    60.00      0.000183      1,640           99.75      0.001770        169
    70.00      0.000241      1,243           99.90      0.001811        166
    80.00      0.000336        893


  ESTIMATED PERCENTILE OF PER-CAPITA DAYS LESS THAN/EQUAL TO CALCULATED
EXPOSURE
     in mg/kg body-wt/day and corresponding Margin of Exposure (MOE)

 PERCENTILE    EXPOSURE    MOE 2/         PERCENTILE    EXPOSURE    MOE
 ----------  ----------  ---------        ----------  ----------  ---------
    10.00      0.000022     13,591           90.00      0.000530        566
    20.00      0.000038      7,918           95.00      0.000837        358
    30.00      0.000043      6,937           97.50      0.001033        290
    40.00      0.000051      5,837           99.00      0.001269        236
    50.00      0.000094      3,192           99.50      0.001685        178
    60.00      0.000170      1,764           99.75      0.001767        170
    70.00      0.000234      1,281           99.90      0.001810        166
    80.00      0.000328        914
```

ACUTE EXPOSURE (EX4) ANALYSIS FOR METHIDATHION
Residue file name: METHIAT1 Analysis date: 06-14-2000
1989-92 DATA Adjustment factor #2 NOT used
DPR NOEL (Acute) = 0.300000 mg/kg body-wt/day

FEMALES (13+/PREG/NOT NSG)

Daily Exposure Analysis (mg/kg body-weight/day)

	per Capita	per User
Mean	0.000095	0.000095
Standard Deviation	0.000127	0.000127
Standard Error	0.000006	0.000006

Percent of Person-Days that are User-Days =100.00%

ESTIMATED PERCENTILE OF USER-DAYS LESS THAN/EQUAL TO CALCULATED EXPOSURE
in mg/kg body-wt/day and corresponding Margin of Exposure (MOE)

PERCENTILE	EXPOSURE	MOE 2/	PERCENTILE	EXPOSURE	MOE
10.00	0.000005	55,787	90.00	0.000264	1,134
20.00	0.000010	31,383	95.00	0.000356	842
30.00	0.000018	16,967	97.50	0.000456	658
40.00	0.000026	11,724	99.00	0.000501	599
50.00	0.000034	8,892	99.50	0.000602	498
60.00	0.000047	6,328	99.75	0.000749	400
70.00	0.000110	2,732	99.90	0.000932	322
80.00	0.000184	1,633			

ESTIMATED PERCENTILE OF PER-CAPITA DAYS LESS THAN/EQUAL TO CALCULATED EXPOSURE
in mg/kg body-wt/day and corresponding Margin of Exposure (MOE)

PERCENTILE	EXPOSURE	MOE 2/	PERCENTILE	EXPOSURE	MOE
10.00	0.000005	55,787	90.00	0.000264	1,134
20.00	0.000010	31,383	95.00	0.000356	842
30.00	0.000018	16,967	97.50	0.000456	658
40.00	0.000026	11,724	99.00	0.000501	599
50.00	0.000034	8,892	99.50	0.000602	498
60.00	0.000047	6,328	99.75	0.000749	400
70.00	0.000110	2,732	99.90	0.000932	322
80.00	0.000184	1,633			

ACUTE EXPOSURE (EX4) ANALYSIS FOR METHIDATHION
Residue file name: METHIAT1 Analysis date: 06-14-2000
1989-92 DATA Adjustment factor #2 NOT used
DPR NOEL (Acute) = 0.300000 mg/kg body-wt/day

FEMALES (13+/NURSING)

	Daily Exposure Analysis (mg/kg body-weight/day) per Capita	per User
Mean	0.000127	0.000127
Standard Deviation	0.000172	0.000172
Standard Error	0.000012	0.000012

Percent of Person-Days that are User-Days =100.00%

ESTIMATED PERCENTILE OF USER-DAYS LESS THAN/EQUAL TO CALCULATED EXPOSURE
in mg/kg body-wt/day and corresponding Margin of Exposure (MOE)

PERCENTILE	EXPOSURE	MOE 2/	PERCENTILE	EXPOSURE	MOE
10.00	0.000005	65,536	90.00	0.000426	704
20.00	0.000007	45,499	95.00	0.000496	604
30.00	0.000012	24,008	97.50	0.000563	533
40.00	0.000021	14,068	99.00	0.000723	415
50.00	0.000032	9,311	99.50	0.000769	390
60.00	0.000079	3,820	99.75	0.000855	351
70.00	0.000152	1,978	99.90	0.000925	324
80.00	0.000238	1,263			

ESTIMATED PERCENTILE OF PER-CAPITA DAYS LESS THAN/EQUAL TO CALCULATED EXPOSURE
in mg/kg body-wt/day and corresponding Margin of Exposure (MOE)

PERCENTILE	EXPOSURE	MOE 2/	PERCENTILE	EXPOSURE	MOE
10.00	0.000005	65,536	90.00	0.000426	704
20.00	0.000007	45,499	95.00	0.000496	604
30.00	0.000012	24,008	97.50	0.000563	533
40.00	0.000021	14,068	99.00	0.000723	415
50.00	0.000032	9,311	99.50	0.000769	390
60.00	0.000079	3,820	99.75	0.000855	351
70.00	0.000152	1,978	99.90	0.000925	324
80.00	0.000238	1,263			

ACUTE EXPOSURE (EX4) ANALYSIS FOR METHIDATHION
Residue file name: METHIAT1 Analysis date: 06-14-2000
1989-92 DATA Adjustment factor #2 NOT used
DPR NOEL (Acute) = 0.300000 mg/kg body-wt/day

CHILDREN (1-6 YEARS)

Daily Exposure Analysis (mg/kg body-weight/day)

	per Capita	per User
Mean	0.000290	0.000290
Standard Deviation	0.000379	0.000379
Standard Error	0.000006	0.000006

Percent of Person-Days that are User-Days = 99.93%

ESTIMATED PERCENTILE OF USER-DAYS LESS THAN/EQUAL TO CALCULATED EXPOSURE
in mg/kg body-wt/day and corresponding Margin of Exposure (MOE)

PERCENTILE	EXPOSURE	MOE 2/	PERCENTILE	EXPOSURE	MOE
10.00	0.000021	14,065	90.00	0.000770	390
20.00	0.000033	9,011	95.00	0.001048	286
30.00	0.000049	6,171	97.50	0.001309	229
40.00	0.000075	3,992	99.00	0.001697	177
50.00	0.000119	2,511	99.50	0.002134	141
60.00	0.000202	1,485	99.75	0.002393	125
70.00	0.000335	894	99.90	0.002668	112
80.00	0.000527	569			

ESTIMATED PERCENTILE OF PER-CAPITA DAYS LESS THAN/EQUAL TO CALCULATED EXPOSURE
in mg/kg body-wt/day and corresponding Margin of Exposure (MOE)

PERCENTILE	EXPOSURE	MOE 2/	PERCENTILE	EXPOSURE	MOE
10.00	0.000021	14,148	90.00	0.000769	390
20.00	0.000033	9,028	95.00	0.001047	286
30.00	0.000049	6,180	97.50	0.001309	229
40.00	0.000075	3,998	99.00	0.001697	177
50.00	0.000119	2,514	99.50	0.002134	141
60.00	0.000202	1,487	99.75	0.002393	125
70.00	0.000335	895	99.90	0.002668	112
80.00	0.000527	569			

ACUTE EXPOSURE (EX4) ANALYSIS FOR METHIDATHION
Residue file name: METHIAT1 Analysis date: 06-14-2000
1989-92 DATA Adjustment factor #2 NOT used
DPR NOEL (Acute) = 0.300000 mg/kg body-wt/day

CHILDREN (7-12 YEARS)

Daily Exposure Analysis (mg/kg body-weight/day)

	per Capita	per User
Mean	0.000165	0.000165
Standard Deviation	0.000231	0.000231
Standard Error	0.000004	0.000004

Percent of Person-Days that are User-Days = 99.98%

ESTIMATED PERCENTILE OF USER-DAYS LESS THAN/EQUAL TO CALCULATED EXPOSURE
in mg/kg body-wt/day and corresponding Margin of Exposure (MOE)

PERCENTILE	EXPOSURE	MOE 2/	PERCENTILE	EXPOSURE	MOE
10.00	0.000012	24,174	90.00	0.000445	675
20.00	0.000020	14,837	95.00	0.000564	532
30.00	0.000031	9,721	97.50	0.000772	389
40.00	0.000047	6,421	99.00	0.001151	261
50.00	0.000067	4,480	99.50	0.001321	227
60.00	0.000104	2,879	99.75	0.001658	181
70.00	0.000169	1,775	99.90	0.001975	152
80.00	0.000293	1,026			

ESTIMATED PERCENTILE OF PER-CAPITA DAYS LESS THAN/EQUAL TO CALCULATED EXPOSURE
in mg/kg body-wt/day and corresponding Margin of Exposure (MOE)

PERCENTILE	EXPOSURE	MOE 2/	PERCENTILE	EXPOSURE	MOE
10.00	0.000012	24,227	90.00	0.000445	675
20.00	0.000020	14,848	95.00	0.000564	532
30.00	0.000031	9,727	97.50	0.000772	389
40.00	0.000047	6,424	99.00	0.001151	261
50.00	0.000067	4,481	99.50	0.001321	227
60.00	0.000104	2,880	99.75	0.001658	181
70.00	0.000169	1,776	99.90	0.001975	152
80.00	0.000292	1,026			

ACUTE EXPOSURE (EX4) ANALYSIS FOR METHIDATHION
Residue file name: METHIAT1 Analysis date: 06-14-2000
1989-92 DATA Adjustment factor #2 NOT used
DPR NOEL (Acute) = 0.300000 mg/kg body-wt/day

MALES (13-19 YEARS)

Daily Exposure Analysis (mg/kg body-weight/day)

	per Capita	per User
Mean	0.000098	0.000098
Standard Deviation	0.000147	0.000147
Standard Error	0.000004	0.000004

Percent of Person-Days that are User-Days = 99.98%

ESTIMATED PERCENTILE OF USER-DAYS LESS THAN/EQUAL TO CALCULATED EXPOSURE
in mg/kg body-wt/day and corresponding Margin of Exposure (MOE)

PERCENTILE	EXPOSURE	MOE 2/	PERCENTILE	EXPOSURE	MOE
10.00	0.000007	43,716	90.00	0.000266	1,129
20.00	0.000011	27,337	95.00	0.000374	801
30.00	0.000016	18,996	97.50	0.000468	641
40.00	0.000023	13,213	99.00	0.000596	503
50.00	0.000032	9,468	99.50	0.000746	402
60.00	0.000051	5,862	99.75	0.000954	314
70.00	0.000095	3,169	99.90	0.001028	292
80.00	0.000200	1,503			

ESTIMATED PERCENTILE OF PER-CAPITA DAYS LESS THAN/EQUAL TO CALCULATED EXPOSURE
in mg/kg body-wt/day and corresponding Margin of Exposure (MOE)

PERCENTILE	EXPOSURE	MOE 2/	PERCENTILE	EXPOSURE	MOE
10.00	0.000007	43,791	90.00	0.000266	1,129
20.00	0.000011	27,352	95.00	0.000374	802
30.00	0.000016	19,004	97.50	0.000468	641
40.00	0.000023	13,217	99.00	0.000596	503
50.00	0.000032	9,471	99.50	0.000745	402
60.00	0.000051	5,864	99.75	0.000954	314
70.00	0.000095	3,170	99.90	0.001028	292
80.00	0.000200	1,503			

ACUTE EXPOSURE (EX4) ANALYSIS FOR METHIDATHION
Residue file name: METHIAT1 Analysis date: 06-14-2000
1989-92 DATA Adjustment factor #2 NOT used
DPR NOEL (Acute) = 0.300000 mg/kg body-wt/day

FEMALES (13-19 YRS/NP/NN)

	Daily Exposure Analysis (mg/kg body-weight/day) per Capita	per User
Mean	0.000086	0.000086
Standard Deviation	0.000134	0.000134
Standard Error	0.000003	0.000003

Percent of Person-Days that are User-Days = 99.71%

ESTIMATED PERCENTILE OF USER-DAYS LESS THAN/EQUAL TO CALCULATED EXPOSURE
in mg/kg body-wt/day and corresponding Margin of Exposure (MOE)

PERCENTILE	EXPOSURE	MOE 2/	PERCENTILE	EXPOSURE	MOE
10.00	0.000004	70,729	90.00	0.000263	1,139
20.00	0.000007	41,005	95.00	0.000358	837
30.00	0.000011	27,593	97.50	0.000473	635
40.00	0.000016	18,928	99.00	0.000582	516
50.00	0.000024	12,404	99.50	0.000705	425
60.00	0.000037	8,023	99.75	0.000817	367
70.00	0.000071	4,242	99.90	0.001067	281
80.00	0.000156	1,921			

ESTIMATED PERCENTILE OF PER-CAPITA DAYS LESS THAN/EQUAL TO CALCULATED EXPOSURE
in mg/kg body-wt/day and corresponding Margin of Exposure (MOE)

PERCENTILE	EXPOSURE	MOE 2/	PERCENTILE	EXPOSURE	MOE
10.00	0.000004	72,634	90.00	0.000263	1,140
20.00	0.000007	41,411	95.00	0.000358	838
30.00	0.000011	27,778	97.50	0.000472	635
40.00	0.000016	19,033	99.00	0.000582	516
50.00	0.000024	12,467	99.50	0.000705	426
60.00	0.000037	8,056	99.75	0.000816	367
70.00	0.000070	4,260	99.90	0.001067	281
80.00	0.000156	1,927			

ACUTE EXPOSURE (EX4) ANALYSIS FOR METHIDATHION
Residue file name: METHIAT1 Analysis date: 06-14-2000
1989-92 DATA Adjustment factor #2 NOT used
DPR NOEL (Acute) = 0.300000 mg/kg body-wt/day

MALES (20+ YEARS)

	Daily Exposure Analysis (mg/kg body-weight/day) per Capita	per User
Mean	0.000064	0.000064
Standard Deviation	0.000099	0.000099
Standard Error	0.000001	0.000001

Percent of Person-Days that are User-Days = 99.75%

ESTIMATED PERCENTILE OF USER-DAYS LESS THAN/EQUAL TO CALCULATED EXPOSURE
in mg/kg body-wt/day and corresponding Margin of Exposure (MOE)

PERCENTILE	EXPOSURE	MOE 2/	PERCENTILE	EXPOSURE	MOE
10.00	0.000003	90,518	90.00	0.000190	1,582
20.00	0.000006	51,576	95.00	0.000253	1,186
30.00	0.000009	32,749	97.50	0.000330	908
40.00	0.000014	21,655	99.00	0.000425	707
50.00	0.000021	14,110	99.50	0.000512	586
60.00	0.000033	9,129	99.75	0.000664	452
70.00	0.000057	5,283	99.90	0.000851	352
80.00	0.000116	2,587			

ESTIMATED PERCENTILE OF PER-CAPITA DAYS LESS THAN/EQUAL TO CALCULATED EXPOSURE
in mg/kg body-wt/day and corresponding Margin of Exposure (MOE)

PERCENTILE	EXPOSURE	MOE 2/	PERCENTILE	EXPOSURE	MOE
10.00	0.000003	92,617	90.00	0.000190	1,583
20.00	0.000006	52,027	95.00	0.000253	1,187
30.00	0.000009	32,961	97.50	0.000330	909
40.00	0.000014	21,767	99.00	0.000424	707
50.00	0.000021	14,172	99.50	0.000512	586
60.00	0.000033	9,161	99.75	0.000664	452
70.00	0.000057	5,300	99.90	0.000851	353
80.00	0.000116	2,593			

ACUTE EXPOSURE (EX4) ANALYSIS FOR METHIDATHION
Residue file name: METHIAT1 Analysis date: 06-14-2000
1989-92 DATA Adjustment factor #2 NOT used
DPR NOEL (Acute) = 0.300000 mg/kg body-wt/day

FEMALES (20+ YEARS/NP/NN)

Daily Exposure Analysis (mg/kg body-weight/day)

	per Capita	per User
Mean	0.000070	0.000070
Standard Deviation	0.000108	0.000108
Standard Error	0.000001	0.000001

Percent of Person-Days that are User-Days = 99.71%

ESTIMATED PERCENTILE OF USER-DAYS LESS THAN/EQUAL TO CALCULATED EXPOSURE
in mg/kg body-wt/day and corresponding Margin of Exposure (MOE)

PERCENTILE	EXPOSURE	MOE 2/	PERCENTILE	EXPOSURE	MOE
10.00	0.000003	96,717	90.00	0.000214	1,404
20.00	0.000006	53,342	95.00	0.000276	1,088
30.00	0.000009	33,889	97.50	0.000353	850
40.00	0.000014	21,309	99.00	0.000482	622
50.00	0.000023	13,061	99.50	0.000579	518
60.00	0.000036	8,331	99.75	0.000716	419
70.00	0.000063	4,760	99.90	0.000832	361
80.00	0.000128	2,338			

ESTIMATED PERCENTILE OF PER-CAPITA DAYS LESS THAN/EQUAL TO CALCULATED EXPOSURE
in mg/kg body-wt/day and corresponding Margin of Exposure (MOE)

PERCENTILE	EXPOSURE	MOE 2/	PERCENTILE	EXPOSURE	MOE
10.00	0.000003	99,338	90.00	0.000213	1,406
20.00	0.000006	53,909	95.00	0.000276	1,089
30.00	0.000009	34,145	97.50	0.000353	850
40.00	0.000014	21,449	99.00	0.000482	622
50.00	0.000023	13,135	99.50	0.000579	519
60.00	0.000036	8,366	99.75	0.000716	419
70.00	0.000063	4,778	99.90	0.000832	361
80.00	0.000128	2,345			

ACUTE EXPOSURE (EX4) ANALYSIS FOR METHIDATHION
Residue file name: METHIAT1 Analysis date: 06-14-2000
1989-92 DATA Adjustment factor #2 NOT used
DPR NOEL (Acute) = 0.300000 mg/kg body-wt/day

SENIORS (55+)

	Daily Exposure Analysis (mg/kg body-weight/day) per Capita	per User
Mean	0.000073	0.000073
Standard Deviation	0.000092	0.000092
Standard Error	0.000001	0.000001

Percent of Person-Days that are User-Days = 99.79%

ESTIMATED PERCENTILE OF USER-DAYS LESS THAN/EQUAL TO CALCULATED EXPOSURE
in mg/kg body-wt/day and corresponding Margin of Exposure (MOE)

PERCENTILE	EXPOSURE	MOE 2/	PERCENTILE	EXPOSURE	MOE
10.00	0.000004	80,602	90.00	0.000206	1,459
20.00	0.000007	45,000	95.00	0.000262	1,144
30.00	0.000011	26,225	97.50	0.000315	952
40.00	0.000020	15,287	99.00	0.000380	788
50.00	0.000031	9,824	99.50	0.000437	686
60.00	0.000049	6,110	99.75	0.000508	591
70.00	0.000090	3,323	99.90	0.000584	514
80.00	0.000142	2,116			

ESTIMATED PERCENTILE OF PER-CAPITA DAYS LESS THAN/EQUAL TO CALCULATED EXPOSURE
in mg/kg body-wt/day and corresponding Margin of Exposure (MOE)

PERCENTILE	EXPOSURE	MOE 2/	PERCENTILE	EXPOSURE	MOE
10.00	0.000004	82,165	90.00	0.000206	1,460
20.00	0.000007	45,338	95.00	0.000262	1,145
30.00	0.000011	26,388	97.50	0.000315	952
40.00	0.000020	15,368	99.00	0.000380	789
50.00	0.000030	9,861	99.50	0.000437	687
60.00	0.000049	6,130	99.75	0.000508	591
70.00	0.000090	3,333	99.90	0.000584	514
80.00	0.000142	2,119			

ACUTE EXPOSURE (EX4) ANALYSIS FOR METHIDATHION
Residue file name: METHIAT1 Analysis date: 06-14-2000
1989-92 DATA Adjustment factor #2 NOT used
DPR NOEL (Acute) = 0.300000 mg/kg body-wt/day

CUSTOM DEMOGRAPHICS 1: Workers, 16+ yrs
All Seasons
All Regions
Sex: M/F-all/
All Races
Age-Low: 16 yrs High: 110 yrs

	Daily Exposure Analysis (mg/kg body-weight/day) per Capita	per User
Mean	0.000069	0.000069
Standard Deviation	0.000106	0.000106
Standard Error	0.000001	0.000001

Percent of Person-Days that are User-Days = 99.74%

ESTIMATED PERCENTILE OF USER-DAYS LESS THAN/EQUAL TO CALCULATED EXPOSURE
in mg/kg body-wt/day and corresponding Margin of Exposure (MOE)

PERCENTILE	EXPOSURE	MOE 2/	PERCENTILE	EXPOSURE	MOE
10.00	0.000003	91,039	90.00	0.000209	1,438
20.00	0.000006	51,036	95.00	0.000272	1,102
30.00	0.000009	32,455	97.50	0.000350	858
40.00	0.000014	20,810	99.00	0.000466	643
50.00	0.000023	13,209	99.50	0.000575	522
60.00	0.000035	8,515	99.75	0.000700	429
70.00	0.000061	4,918	99.90	0.000882	340
80.00	0.000126	2,375			

ESTIMATED PERCENTILE OF PER-CAPITA DAYS LESS THAN/EQUAL TO CALCULATED EXPOSURE in mg/kg body-wt/day and corresponding Margin of Exposure (MOE)

PERCENTILE	EXPOSURE	MOE 2/	PERCENTILE	EXPOSURE	MOE
10.00	0.000003	93,232	90.00	0.000208	1,439
20.00	0.000006	51,509	95.00	0.000272	1,103
30.00	0.000009	32,673	97.50	0.000350	858
40.00	0.000014	20,928	99.00	0.000466	644
50.00	0.000023	13,272	99.50	0.000575	522
60.00	0.000035	8,547	99.75	0.000699	429
70.00	0.000061	4,934	99.90	0.000882	340
80.00	0.000126	2,382			

Chronic Exposure (EX1) Analysis for methidathion
RESIDUE FILE NAME: METHICT2 ANALYSIS DATE: 05-27-1999
NFCS Combined 89-92 DATA ADJUSTMENT FACTOR #2 NOT USED
EPA Reference dose (RfD, chronic) = 0.001500 mg/kg body-wt/day
DPR NOEL (Chronic) = 0.150000 mg/kg body-wt/day
COMMENT 1: Tier 2 Analysis - DPR + PDP monitoring data

RESIDUE FILE LISTING

TAS CODE	CROP GRP	FOOD NAME	RESIDUE (PPM)	ADJ. FCTRS #1	ADJ. FCTRS #2	SOURCE CODE
20	K	CITRUS CITRON	0.001820	25.00	1.00	PDP-OR
22	K	GRAPEFRUIT-PEELED FRUIT	0.011000	0.10	1.00	DPR
23	K	GRAPEFRUIT-JUICE	0.011000	0.10	1.00	DPR
24	K	KUMQUATS	0.005000	1.00	1.00	DPR
26	K	LEMONS-PEELED FRUIT	0.007000	0.10	1.00	DPR
27	K	LEMONS-PEEL	0.007000	2.50	1.00	DPR
28	K	LEMONS-JUICE	0.007000	0.10	1.00	DPR
30	K	LIMES-PEELED FRUIT	0.006000	0.10	1.00	DPR
31	K	LIMES-PEEL	0.006000	2.50	1.00	DPR
32	K	LIMES-JUICE	0.006000	0.10	1.00	DPR
33	K	ORANGES-JUICE-CONCENTRATE	0.001550	1.00	1.00	PDP
34	K	ORANGES-PEELED FRUIT	0.001820	1.00	1.00	PDP95%
35	K	ORANGES-PEEL	0.001820	25.00	1.00	PDP95%
36	K	ORANGES-JUICE	0.001550	1.00	1.00	PDP
37	K	TANGELOS	0.005000	0.10	1.00	DPR
38	K	TANGERINES	0.015000	0.10	1.00	DPR
39	K	TANGERINES-JUICE	0.015000	0.10	1.00	DPR
40	R	ALMONDS	0.025000	1.00	1.00	1/2TOL
41	R	BRAZIL NUTS	0.025000	1.00	1.00	1/2TOL
42	R	CASHEWS	0.025000	1.00	1.00	1/2TOL
43	R	CHESTNUTS	0.025000	1.00	1.00	1/2TOL
44	R	FILBERTS (HAZELNUTS)	0.025000	1.00	1.00	1/2TOL
45	R	HICKORY NUTS	0.025000	1.00	1.00	1/2TOL
46	R	MACADAMIA NUTS (BUSH NUTS)	0.025000	1.00	1.00	1/2TOL
47	R	PECANS	0.025000	1.00	1.00	1/2TOL
48	R	WALNUTS	0.025000	1.00	1.00	1/2TOL
49	R	BUTTER NUTS	0.025000	1.00	1.00	1/2TOL
50	A	PISTACHIO NUTS	0.025000	1.00	1.00	1/2TOL
51	R	BEECHNUTS	0.025000	1.00	1.00	1/2TOL
52	L	APPLES	0.005000	1.00	1.00	PDP
53	L	APPLES-DRIED	0.005000	8.00	1.00	PDP
54	L	APPLES-JUICE/CIDER	0.001500	1.30	1.00	PDP
55	L	CRABAPPLES	0.005000	1.00	1.00	PDP-AP
56	L	PEARS	0.005000	1.00	1.00	PDP
57	L	PEARS-DRIED	0.005000	6.25	1.00	PDP
58	L	QUINCES	0.005000	1.00	1.00	DPR
59	M	APRICOTS	0.005000	1.00	1.00	DPR
60	M	APRICOTS-DRIED	0.005000	6.00	1.00	DPR
61	M	CHERRIES	0.005000	1.00	1.00	DPR

TAS CODE	CROP GRP	FOOD NAME	RESIDUE (PPM)	ADJ. FCTRS #1	ADJ. FCTRS #2	SOURCE CODE
62	M	CHERRIES-DRIED	0.005000	4.00	1.00	DPR
63	M	CHERRIES-JUICE	0.005000	1.50	1.00	DPR
64	M	NECTARINES	0.005000	1.00	1.00	DPR
65	M	PEACHES	0.001500	1.00	1.00	PDP
66	M	PEACHES-DRIED	0.001500	7.00	1.00	PDP
67	M	PLUMS(DAMSONS)	0.005000	1.00	1.00	DPR
68	M	PLUMS-PRUNES(DRIED)	0.005000	5.00	1.00	DPR
69	M	PLUMS/PRUNE-JUICE	0.005000	1.40	1.00	DPR
80	A	MANGOES	0.025000	1.00	1.00	1/2TOL
82	A	OLIVES	0.025000	1.00	1.00	1/2TOL
97	A	KIWI FRUIT	0.005000	1.00	1.00	DPR
103	A	SUGAR APPLES (SWEETSOP)	0.100000	1.00	1.00	1/2TOL
106	A	CARAMBOLA (STARFRUIT)	0.050000	1.00	1.00	1/2TOL
108	A	LONGAN FRUIT	0.050000	1.00	1.00	1/2TOL
181	A	ARTICHOKES-GLOBE	0.005000	1.00	1.00	DPR
203	B	ARTICHOKES-JERUSALEM	0.005000	1.00	1.00	DPR
246	A	SUNFLOWER-SEEDS-WITH HULLS	0.250000	1.00	1.00	1/2TOL
275	O	SORGHUM (INCLUDING MILO)	0.100000	1.00	1.00	1/2TOL
290	A	COTTONSEED-OIL	0.100000	1.00	1.00	1/2TOL
291	A	COTTONSEED-MEAL	0.100000	1.00	1.00	1/2TOL
294	A	SAFFLOWER-SEED	0.250000	1.00	1.00	1/2TOL
295	A	SAFFLOWER-OIL	0.250000	1.00	1.00	1/2TOL
300	A	OLIVE OIL	0.025000	1.00	1.00	1/2TOL
318	X	MILK-NONFAT SOLIDS	0.000100	7.87	1.00	REGIST
319	X	MILK-FAT SOLIDS	0.000100	7.87	1.00	REGIST
320	X	MILK SUGAR (LACTOSE)	0.000100	8.13	1.00	REGIST
321	U	BEEF-MEAT BYPRODUCTS	0.000270	1.00	1.00	REGIST
322	U	BEEF(ORGAN MEATS)-OTHER	0.000270	1.00	1.00	REGIST
323	U	BEEF-DRIED	0.000270	1.92	1.00	REGIST
324	U	BEEF(BONELESS)-FAT	0.000030	1.00	1.00	REGIST
325	U	BEEF(ORGAN MEATS)-KIDNEY	0.000180	1.00	1.00	REGIST
326	U	BEEF(ORGAN MEATS)-LIVER	0.000270	1.00	1.00	REGIST
327	U	BEEF(BONELESS)-LEAN (FAT/FREE)	0.000270	1.00	1.00	REGIST
328	U	GOAT-MEAT BYPRODUCTS	0.000270	1.00	1.00	REGIST
329	U	GOAT(ORGAN MEATS)-OTHER	0.000270	1.00	1.00	REGIST
330	U	GOAT(BONELESS)-FAT	0.000030	1.00	1.00	REGIST
331	U	GOAT(ORGAN MEATS)-KIDNEY	0.000180	1.00	1.00	REGIST
332	U	GOAT(ORGAN MEATS)-LIVER	0.000270	1.00	1.00	REGIST
333	U	GOAT(BONELESS)-LEAN (FAT/FREE)	0.000270	1.00	1.00	REGIST
334	U	HORSE	0.000270	1.00	1.00	REGIST
336	U	SHEEP-MEAT BYPRODUCTS	0.000270	1.00	1.00	REGIST
337	U	SHEEP(ORGAN MEATS)-OTHER	0.000270	1.00	1.00	REGIST
338	U	SHEEP(BONELESS)-FAT	0.000030	1.00	1.00	REGIST
339	U	SHEEP(ORGAN MEATS)-KIDNEY	0.000180	1.00	1.00	REGIST
340	U	SHEEP(ORGAN MEATS)-LIVER	0.000270	1.00	1.00	REGIST
341	U	SHEEP(BONELESS)-LEAN (FAT FREE	0.000270	1.00	1.00	REGIST
342	U	PORK-MEAT BYPRODUCTS	0.000140	1.00	1.00	REGIST
343	U	PORK(ORGAN MEATS)-OTHER	0.000140	1.00	1.00	REGIST

TAS CODE	CROP GRP	FOOD NAME	RESIDUE (PPM)	ADJ. FCTRS #1	ADJ. FCTRS #2	SOURCE CODE
344	U	PORK(BONELESS)-FAT	0.000010	1.00	1.00	REGIST
345	U	PORK(ORGAN MEATS)-KIDNEY	0.000090	1.00	1.00	REGIST
346	U	PORK(ORGAN MEATS)-LIVER	0.000140	1.00	1.00	REGIST
347	U	PORK(BONELESS)-LEAN (FAT FREE)	0.000140	1.00	1.00	REGIST
355	V	TURKEY-BYPRODUCTS	0.000090	1.00	1.00	REGIST
356	V	TURKEY-GIBLETS (LIVER)	0.000090	1.00	1.00	REGIST
357	V	TURKEY-(BONELESS)-FAT	0.000030	1.00	1.00	REGIST
358	V	TURKEY-(BONELESS)LEAN/FAT FREE	0.000040	1.00	1.00	REGIST
359	V	TURKEY-UNSPECIFIED	0.000090	1.00	1.00	REGIST
360	V	POULTRY-OTHER-LEAN (FAT FREE)	0.000040	1.00	1.00	REGIST
361	V	POULTRY-OTHER-GIBLETS(LIVER)	0.000090	1.00	1.00	REGIST
362	V	POULTRY-OTHER-FAT	0.000030	1.00	1.00	REGIST
363	X	EGGS-WHOLE	0.000050	1.00	1.00	REGIST
364	X	EGGS-WHITE ONLY	0.000050	1.00	1.00	REGIST
365	X	EGGS-YOLK ONLY	0.000050	1.00	1.00	REGIST
366	V	CHICKEN-BYPRODUCTS	0.000090	1.00	1.00	REGIST
367	V	CHICKEN-GIBLETS(LIVER)	0.000090	1.00	1.00	REGIST
368	V	CHICKEN (BONELESS)-FAT	0.000030	1.00	1.00	REGIST
369	V	CHICKEN(BONELESS)LEAN/FAT FREE	0.000040	1.00	1.00	REGIST
377	L	APPLES-JUICE-CONCENTRATE	0.001500	3.90	1.00	PDP
385	V	CHICKEN-GIBLETS (EXCL. LIVER)	0.000090	1.00	1.00	REGIST
398	X	MILK-BASED WATER	0.000100	1.00	1.00	REGIST
402	M	PEACHES-JUICE	0.001500	1.00	1.00	PDP
404	L	PEARS-NECTAR	0.005000	1.00	1.00	PDP
410	M	APRICOT JUICE OR NECTAR	0.005000	1.00	1.00	DPR
417	A	SUNFLOWER-SEEDS-HULLED	0.250000	1.00	1.00	1/2TOL
420	K	TANGERINES-JUICE-CONCENTRATE	0.015000	0.32	1.00	DPR
424	U	VEAL-(BONELESS)-FAT	0.000030	1.00	1.00	REGIST
425	U	VEAL-(BONELESS)-LEAN (FAT FREE	0.000270	1.00	1.00	REGIST
426	U	VEAL-(ORGAN MEATS)-KIDNEY	0.000180	1.00	1.00	REGIST
427	U	VEAL-(ORGAN MEATS)-LIVER	0.000270	1.00	1.00	REGIST
428	U	VEAL-(ORGAN MEATS)-OTHER	0.000270	1.00	1.00	REGIST
429	U	VEAL-DRIED	0.000270	1.92	1.00	REGIST
430	U	VEAL-MEAT BYPRODUCTS	0.000270	1.00	1.00	REGIST
431	R	WALNUT OIL	0.025000	1.00	1.00	1/2TOL
441	K	GRAPEFRUIT-JUICE-CONCENTRATE	0.011000	0.39	1.00	DPR
442	K	LEMONS-JUICE-CONCENTRATE	0.007000	0.57	1.00	DPR
443	K	LIMES-JUICE-CONCENTRATE	0.006000	0.30	1.00	DPR
448	K	GRAPEFRUIT PEEL	0.014000	2.50	1.00	DPR
449	V	TURKEY-(ORGAN MEATS)-OTHER	0.000080	1.00	1.00	REGIST

Chronic Exposure (EX1) Analysis for methidathion
RESIDUE FILE NAME: METHICT1 ANALYSIS DATE: 05-27-1999
NFCS Combined 89-92 DATA ADJUSTMENT FACTOR #2 NOT USED
EPA Reference dose (RfD, chronic) = 0.001500 mg/kg body-wt/day
DPR NOEL (Chronic) = 0.150000 mg/kg body-wt/day
COMMENT 1: Tier 1 Analysis - DPR monitoring data

TOTAL EXPOSURE BY POPULATION SUBGROUP

POPULATION SUBGROUP	TOTAL EXPOSURE mg/kg body-wt/day	Margin of Exposure 1/	Percent of RfD
U.S. POP - 48 STATES - ALL SEASONS	0.000034	4,398	2.3%
U.S. POPULATION - SPRING SEASON	0.000032	4,708	2.1%
U.S. POPULATION - SUMMER SEASON	0.000033	4,484	2.2%
U.S. POPULATION - AUTUMN SEASON	0.000035	4,255	2.4%
U.S. POPULATION - WINTER SEASON	0.000036	4,198	2.4%
NORTHEAST REGION	0.000038	3,920	2.6%
MIDWEST REGION	0.000033	4,602	2.2%
SOUTHERN REGION	0.000031	4,832	2.1%
WESTERN REGION	0.000037	4,067	2.5%
PACIFIC REGION	0.000038	3,937	2.5%
HISPANICS	0.000037	4,001	2.5%
NON-HISPANIC WHITES	0.000033	4,532	2.2%
NON-HISPANIC BLACKS	0.000036	4,211	2.4%
NON-HISPANIC OTHER THAN BLACK OR WHITE	0.000046	3,244	3.1%
ALL INFANTS	0.000070	2,142	4.7%
NURSING INFANTS (<1 YEAR OLD)	0.000045	3,320	3.0%
NON-NURSING INFANTS (<1 YEAR OLD)	0.000080	1,864	5.4%
CHILDREN (1-6 YEARS)	0.000098	1,527	6.5%
CHILDREN (7-12 YEARS)	0.000056	2,672	3.7%
FEMALES (13-19 YRS/NOT PREG. OR NURSING)	0.000028	5,368	1.9%
FEMALES (20+ YEARS/NOT PREG. OR NURSING)	0.000023	6,478	1.5%
FEMALES (13-50 YEARS)	0.000024	6,213	1.6%
FEMALES (13+/PREGNANT/NOT NURSING)	0.000032	4,728	2.1%
FEMALES (13+/NURSING)	0.000043	3,493	2.9%
MALES (13-19 YEARS)	0.000032	4,633	2.2%
MALES (20+ YEARS)	0.000021	7,041	1.4%
SENIORS (55+)	0.000023	6,454	1.5%

1. Margin of Exposure = DPR NOEL / Dietary Exposure

Chronic Exposure (EX1) Analysis for methidathion
RESIDUE FILE NAME: METHICT1 ANALYSIS DATE: 06-21-2000
NFCS Combined 89-92 DATA
Q_1 = 0.340000
COMMENT 1: Tier 1 Analysis - DPR monitoring data

TOTAL EXPOSURE BY POPULATION SUBGROUP

POPULATION SUBGROUP	TOTAL EXPOSURE mg/kg body-wt/day	TOTAL EXPOSURE Life-Time Risk (Q_1=0.340000)
U.S. POP - 48 STATES - ALL SEASONS	0.000034	1.16E-05
U.S. POPULATION - SPRING SEASON	0.000032	1.08E-05
U.S. POPULATION - SUMMER SEASON	0.000033	1.14E-05
U.S. POPULATION - AUTUMN SEASON	0.000035	1.20E-05
U.S. POPULATION - WINTER SEASON	0.000036	1.21E-05
NORTHEAST REGION	0.000038	1.30E-05
MIDWEST REGION	0.000033	1.11E-05
SOUTHERN REGION	0.000031	1.06E-05
WESTERN REGION	0.000037	1.25E-05
PACIFIC REGION	0.000038	1.30E-05
HISPANICS	0.000037	1.27E-05
NON-HISPANIC WHITES	0.000033	1.13E-05
NON-HISPANIC BLACKS	0.000036	1.21E-05
NON-HISPANIC OTHER THAN BLACK OR WHITE	0.000046	1.57E-05
ALL INFANTS	0.000070	2.38E-05
NURSING INFANTS (<1 YEAR OLD)	0.000045	1.54E-05
NON-NURSING INFANTS (<1 YEAR OLD)	0.000080	2.74E-05
CHILDREN (1-6 YEARS)	0.000098	3.34E-05
CHILDREN (7-12 YEARS)	0.000056	1.91E-05
FEMALES (13-19 YRS/NOT PREG. OR NURSING)	0.000028	9.50E-06
FEMALES (20+ YEARS/NOT PREG. OR NURSING)	0.000023	7.87E-06
FEMALES (13-50 YEARS)	0.000024	8.21E-06
FEMALES (13+/PREGNANT/NOT NURSING)	0.000032	1.08E-05
FEMALES (13+/NURSING)	0.000043	1.46E-05
MALES (13-19 YEARS)	0.000032	1.10E-05
MALES (20+ YEARS)	0.000021	7.24E-06
SENIORS (55+)	0.000023	7.90E-06

Chronic Exposure (EX1) Analysis for methidathion
RESIDUE FILE NAME: METHICT1 ANALYSIS DATE: 06-21-2000
NFCS Combined 89-92 DATA
Q_1* = 0.530000
COMMENT 1: Tier 1 Analysis - DPR monitoring data

TOTAL EXPOSURE BY POPULATION SUBGROUP

POPULATION SUBGROUP	TOTAL EXPOSURE mg/kg body-wt/day	TOTAL EXPOSURE Life-Time Risk (Q_1*=0.530000)
U.S. POP - 48 STATES - ALL SEASONS	0.000034	1.81E-05
U.S. POPULATION - SPRING SEASON	0.000032	1.69E-05
U.S. POPULATION - SUMMER SEASON	0.000033	1.77E-05
U.S. POPULATION - AUTUMN SEASON	0.000035	1.87E-05
U.S. POPULATION - WINTER SEASON	0.000036	1.89E-05
NORTHEAST REGION	0.000038	2.03E-05
MIDWEST REGION	0.000033	1.73E-05
SOUTHERN REGION	0.000031	1.65E-05
WESTERN REGION	0.000037	1.95E-05
PACIFIC REGION	0.000038	2.02E-05
HISPANICS	0.000037	1.99E-05
NON-HISPANIC WHITES	0.000033	1.75E-05
NON-HISPANIC BLACKS	0.000036	1.89E-05
NON-HISPANIC OTHER THAN BLACK OR WHITE	0.000046	2.45E-05
ALL INFANTS	0.000070	3.71E-05
NURSING INFANTS (<1 YEAR OLD)	0.000045	2.39E-05
NON-NURSING INFANTS (<1 YEAR OLD)	0.000080	4.27E-05
CHILDREN (1-6 YEARS)	0.000098	5.21E-05
CHILDREN (7-12 YEARS)	0.000056	2.98E-05
FEMALES (13-19 YRS/NOT PREG. OR NURSING)	0.000028	1.48E-05
FEMALES (20+ YEARS/NOT PREG. OR NURSING)	0.000023	1.23E-05
FEMALES (13-50 YEARS)	0.000024	1.28E-05
FEMALES (13+/PREGNANT/NOT NURSING)	0.000032	1.68E-05
FEMALES (13+/NURSING)	0.000043	2.28E-05
MALES (13-19 YEARS)	0.000032	1.72E-05
MALES (20+ YEARS)	0.000021	1.13E-05
SENIORS (55+)	0.000023	1.23E-05

Chronic Exposure (EX1) Analysis for methidathion
RESIDUE FILE NAME: METHICT2 ANALYSIS DATE: 05-27-1999
NFCS Combined 89-92 DATA ADJUSTMENT FACTOR #2 NOT USED
EPA Reference dose (RfD, chronic) = 0.001500 mg/kg body-wt/day
DPR NOEL (Chronic) = 0.150000 mg/kg body-wt/day
COMMENT 1: Tier 2 Analysis - DPR + PDP monitoring data

RESIDUE FILE LISTING

TAS CODE	CROP GRP	FOOD NAME	RESIDUE (PPM)	ADJ. FCTRS #1	ADJ. FCTRS #2	SOURCE CODE
20	K	CITRUS CITRON	0.001820	25.00	1.00	PDP-OR
22	K	GRAPEFRUIT-PEELED FRUIT	0.011000	0.10	1.00	DPR
23	K	GRAPEFRUIT-JUICE	0.011000	0.10	1.00	DPR
24	K	KUMQUATS	0.005000	1.00	1.00	DPR
26	K	LEMONS-PEELED FRUIT	0.007000	0.10	1.00	DPR
27	K	LEMONS-PEEL	0.007000	2.50	1.00	DPR
28	K	LEMONS-JUICE	0.007000	0.10	1.00	DPR
30	K	LIMES-PEELED FRUIT	0.006000	0.10	1.00	DPR
31	K	LIMES-PEEL	0.006000	2.50	1.00	DPR
32	K	LIMES-JUICE	0.006000	0.10	1.00	DPR
33	K	ORANGES-JUICE-CONCENTRATE	0.001550	1.00	1.00	PDP
34	K	ORANGES-PEELED FRUIT	0.001820	1.00	1.00	PDP95%
35	K	ORANGES-PEEL	0.001820	25.00	1.00	PDP95%
36	K	ORANGES-JUICE	0.001550	1.00	1.00	PDP
37	K	TANGELOS	0.005000	0.10	1.00	DPR
38	K	TANGERINES	0.015000	0.10	1.00	DPR
39	K	TANGERINES-JUICE	0.015000	0.10	1.00	DPR
40	R	ALMONDS	0.025000	1.00	1.00	1/2TOL
41	R	BRAZIL NUTS	0.025000	1.00	1.00	1/2TOL
42	R	CASHEWS	0.025000	1.00	1.00	1/2TOL
43	R	CHESTNUTS	0.025000	1.00	1.00	1/2TOL
44	R	FILBERTS (HAZELNUTS)	0.025000	1.00	1.00	1/2TOL
45	R	HICKORY NUTS	0.025000	1.00	1.00	1/2TOL
46	R	MACADAMIA NUTS (BUSH NUTS)	0.025000	1.00	1.00	1/2TOL
47	R	PECANS	0.025000	1.00	1.00	1/2TOL
48	R	WALNUTS	0.025000	1.00	1.00	1/2TOL
49	R	BUTTER NUTS	0.025000	1.00	1.00	1/2TOL
50	A	PISTACHIO NUTS	0.025000	1.00	1.00	1/2TOL
51	R	BEECHNUTS	0.025000	1.00	1.00	1/2TOL
52	L	APPLES	0.005000	1.00	1.00	PDP
53	L	APPLES-DRIED	0.005000	8.00	1.00	PDP
54	L	APPLES-JUICE/CIDER	0.001500	1.30	1.00	PDP
55	L	CRABAPPLES	0.005000	1.00	1.00	PDP-AP
56	L	PEARS	0.005000	1.00	1.00	PDP
57	L	PEARS-DRIED	0.005000	6.25	1.00	PDP
58	L	QUINCES	0.005000	1.00	1.00	DPR
59	M	APRICOTS	0.005000	1.00	1.00	DPR
60	M	APRICOTS-DRIED	0.005000	6.00	1.00	DPR
61	M	CHERRIES	0.005000	1.00	1.00	DPR

TAS CODE	CROP GRP	FOOD NAME	RESIDUE (PPM)	ADJ. FCTRS #1	ADJ. FCTRS #2	SOURCE CODE
62	M	CHERRIES-DRIED	0.005000	4.00	1.00	DPR
63	M	CHERRIES-JUICE	0.005000	1.50	1.00	DPR
64	M	NECTARINES	0.005000	1.00	1.00	DPR
65	M	PEACHES	0.001500	1.00	1.00	PDP
66	M	PEACHES-DRIED	0.001500	7.00	1.00	PDP
67	M	PLUMS(DAMSONS)	0.005000	1.00	1.00	DPR
68	M	PLUMS-PRUNES(DRIED)	0.005000	5.00	1.00	DPR
69	M	PLUMS/PRUNE-JUICE	0.005000	1.40	1.00	DPR
80	A	MANGOES	0.025000	1.00	1.00	1/2TOL
82	A	OLIVES	0.025000	1.00	1.00	1/2TOL
97	A	KIWI FRUIT	0.005000	1.00	1.00	DPR
103	A	SUGAR APPLES (SWEETSOP)	0.100000	1.00	1.00	1/2TOL
106	A	CARAMBOLA (STARFRUIT)	0.050000	1.00	1.00	1/2TOL
108	A	LONGAN FRUIT	0.050000	1.00	1.00	1/2TOL
181	A	ARTICHOKES-GLOBE	0.005000	1.00	1.00	DPR
203	B	ARTICHOKES-JERUSALEM	0.005000	1.00	1.00	DPR
246	A	SUNFLOWER-SEEDS-WITH HULLS	0.250000	1.00	1.00	1/2TOL
275	O	SORGHUM (INCLUDING MILO)	0.100000	1.00	1.00	1/2TOL
290	A	COTTONSEED-OIL	0.100000	1.00	1.00	1/2TOL
291	A	COTTONSEED-MEAL	0.100000	1.00	1.00	1/2TOL
294	A	SAFFLOWER-SEED	0.250000	1.00	1.00	1/2TOL
295	A	SAFFLOWER-OIL	0.250000	1.00	1.00	1/2TOL
300	A	OLIVE OIL	0.025000	1.00	1.00	1/2TOL
318	X	MILK-NONFAT SOLIDS	0.000100	7.87	1.00	REGIST
319	X	MILK-FAT SOLIDS	0.000100	7.87	1.00	REGIST
320	X	MILK SUGAR (LACTOSE)	0.000100	8.13	1.00	REGIST
321	U	BEEF-MEAT BYPRODUCTS	0.000270	1.00	1.00	REGIST
322	U	BEEF(ORGAN MEATS)-OTHER	0.000270	1.00	1.00	REGIST
323	U	BEEF-DRIED	0.000270	1.92	1.00	REGIST
324	U	BEEF(BONELESS)-FAT	0.000030	1.00	1.00	REGIST
325	U	BEEF(ORGAN MEATS)-KIDNEY	0.000180	1.00	1.00	REGIST
326	U	BEEF(ORGAN MEATS)-LIVER	0.000270	1.00	1.00	REGIST
327	U	BEEF(BONELESS)-LEAN (FAT/FREE)	0.000270	1.00	1.00	REGIST
328	U	GOAT-MEAT BYPRODUCTS	0.000270	1.00	1.00	REGIST
329	U	GOAT(ORGAN MEATS)-OTHER	0.000270	1.00	1.00	REGIST
330	U	GOAT(BONELESS)-FAT	0.000030	1.00	1.00	REGIST
331	U	GOAT(ORGAN MEATS)-KIDNEY	0.000180	1.00	1.00	REGIST
332	U	GOAT(ORGAN MEATS)-LIVER	0.000270	1.00	1.00	REGIST
333	U	GOAT(BONELESS)-LEAN (FAT/FREE)	0.000270	1.00	1.00	REGIST
334	U	HORSE	0.000270	1.00	1.00	REGIST
336	U	SHEEP-MEAT BYPRODUCTS	0.000270	1.00	1.00	REGIST
337	U	SHEEP(ORGAN MEATS)-OTHER	0.000270	1.00	1.00	REGIST
338	U	SHEEP(BONELESS)-FAT	0.000030	1.00	1.00	REGIST
339	U	SHEEP(ORGAN MEATS)-KIDNEY	0.000180	1.00	1.00	REGIST
340	U	SHEEP(ORGAN MEATS)-LIVER	0.000270	1.00	1.00	REGIST
341	U	SHEEP(BONELESS)-LEAN (FAT FREE	0.000270	1.00	1.00	REGIST
342	U	PORK-MEAT BYPRODUCTS	0.000140	1.00	1.00	REGIST
343	U	PORK(ORGAN MEATS)-OTHER	0.000140	1.00	1.00	REGIST

TAS CODE	CROP GRP	FOOD NAME	RESIDUE (PPM)	ADJ. FCTRS #1	ADJ. FCTRS #2	SOURCE CODE
344	U	PORK(BONELESS)-FAT	0.000010	1.00	1.00	REGIST
345	U	PORK(ORGAN MEATS)-KIDNEY	0.000090	1.00	1.00	REGIST
346	U	PORK(ORGAN MEATS)-LIVER	0.000140	1.00	1.00	REGIST
347	U	PORK(BONELESS)-LEAN (FAT FREE)	0.000140	1.00	1.00	REGIST
355	V	TURKEY-BYPRODUCTS	0.000090	1.00	1.00	REGIST
356	V	TURKEY-GIBLETS (LIVER)	0.000090	1.00	1.00	REGIST
357	V	TURKEY-(BONELESS)-FAT	0.000030	1.00	1.00	REGIST
358	V	TURKEY-(BONELESS)LEAN/FAT FREE	0.000040	1.00	1.00	REGIST
359	V	TURKEY-UNSPECIFIED	0.000090	1.00	1.00	REGIST
360	V	POULTRY-OTHER-LEAN (FAT FREE)	0.000040	1.00	1.00	REGIST
361	V	POULTRY-OTHER-GIBLETS(LIVER)	0.000090	1.00	1.00	REGIST
362	V	POULTRY-OTHER-FAT	0.000030	1.00	1.00	REGIST
363	X	EGGS-WHOLE	0.000050	1.00	1.00	REGIST
364	X	EGGS-WHITE ONLY	0.000050	1.00	1.00	REGIST
365	X	EGGS-YOLK ONLY	0.000050	1.00	1.00	REGIST
366	V	CHICKEN-BYPRODUCTS	0.000090	1.00	1.00	REGIST
367	V	CHICKEN-GIBLETS(LIVER)	0.000090	1.00	1.00	REGIST
368	V	CHICKEN (BONELESS)-FAT	0.000030	1.00	1.00	REGIST
369	V	CHICKEN(BONELESS)LEAN/FAT FREE	0.000040	1.00	1.00	REGIST
377	L	APPLES-JUICE-CONCENTRATE	0.001500	3.90	1.00	PDP
385	V	CHICKEN-GIBLETS (EXCL. LIVER)	0.000090	1.00	1.00	REGIST
398	X	MILK-BASED WATER	0.000100	1.00	1.00	REGIST
402	M	PEACHES-JUICE	0.001500	1.00	1.00	PDP
404	L	PEARS-NECTAR	0.005000	1.00	1.00	PDP
410	M	APRICOT JUICE OR NECTAR	0.005000	1.00	1.00	DPR
417	A	SUNFLOWER-SEEDS-HULLED	0.250000	1.00	1.00	1/2TOL
420	K	TANGERINES-JUICE-CONCENTRATE	0.015000	0.32	1.00	DPR
424	U	VEAL-(BONELESS)-FAT	0.000030	1.00	1.00	REGIST
425	U	VEAL-(BONELESS)-LEAN (FAT FREE	0.000270	1.00	1.00	REGIST
426	U	VEAL-(ORGAN MEATS)-KIDNEY	0.000180	1.00	1.00	REGIST
427	U	VEAL-(ORGAN MEATS)-LIVER	0.000270	1.00	1.00	REGIST
428	U	VEAL-(ORGAN MEATS)-OTHER	0.000270	1.00	1.00	REGIST
429	U	VEAL-DRIED	0.000270	1.92	1.00	REGIST
430	U	VEAL-MEAT BYPRODUCTS	0.000270	1.00	1.00	REGIST
431	R	WALNUT OIL	0.025000	1.00	1.00	1/2TOL
441	K	GRAPEFRUIT-JUICE-CONCENTRATE	0.011000	0.39	1.00	DPR
442	K	LEMONS-JUICE-CONCENTRATE	0.007000	0.57	1.00	DPR
443	K	LIMES-JUICE-CONCENTRATE	0.006000	0.30	1.00	DPR
448	K	GRAPEFRUIT PEEL	0.014000	2.50	1.00	DPR
449	V	TURKEY-(ORGAN MEATS)-OTHER	0.000080	1.00	1.00	REGIST

Chronic Exposure (EX1) Analysis for methidathion
RESIDUE FILE NAME: METHICT2 ANALYSIS DATE: 05-27-1999
NFCS Combined 89-92 DATA ADJUSTMENT FACTOR #2 NOT USED
EPA Reference dose (RfD, chronic) = 0.001500 mg/kg body-wt/day
DPR NOEL (Chronic) = 0.150000 mg/kg body-wt/day
COMMENT 1: Tier 2 Analysis - DPR + PDP monitoring data

TOTAL EXPOSURE BY POPULATION SUBGROUP

POPULATION SUBGROUP	TOTAL EXPOSURE mg/kg body-wt/day	Margin of Exposure 1/	Percent of RfD
U.S. POP - 48 STATES - ALL SEASONS	0.000015	9,815	1.0%
U.S. POPULATION - SPRING SEASON	0.000014	10,666	0.9%
U.S. POPULATION - SUMMER SEASON	0.000015	9,744	1.0%
U.S. POPULATION - AUTUMN SEASON	0.000016	9,282	1.1%
U.S. POPULATION - WINTER SEASON	0.000015	9,738	1.0%
NORTHEAST REGION	0.000016	9,250	1.1%
MIDWEST REGION	0.000016	9,628	1.0%
SOUTHERN REGION	0.000014	10,429	1.0%
WESTERN REGION	0.000016	9,674	1.0%
PACIFIC REGION	0.000015	9,706	1.0%
HISPANICS	0.000013	11,565	0.9%
NON-HISPANIC WHITES	0.000016	9,667	1.0%
NON-HISPANIC BLACKS	0.000015	9,971	1.0%
NON-HISPANIC OTHER THAN BLACK OR WHITE	0.000017	8,843	1.1%
ALL INFANTS	0.000035	4,295	2.3%
NURSING INFANTS (<1 YEAR OLD)	0.000017	8,833	1.1%
NON-NURSING INFANTS (<1 YEAR OLD)	0.000042	3,531	2.8%
CHILDREN (1-6 YEARS)	0.000039	3,893	2.6%
CHILDREN (7-12 YEARS)	0.000026	5,708	1.8%
FEMALES (13-19 YRS/NOT PREG. OR NURSING)	0.000012	12,667	0.8%
FEMALES (20+ YEARS/NOT PREG. OR NURSING)	0.000010	14,589	0.7%
FEMALES (13-50 YEARS)	0.000011	13,851	0.7%
FEMALES (13+/PREGNANT/NOT NURSING)	0.000013	11,297	0.9%
FEMALES (13+/NURSING)	0.000019	8,025	1.2%
MALES (13-19 YEARS)	0.000015	9,994	1.0%
MALES (20+ YEARS)	0.000011	13,835	0.7%
SENIORS (55+)	0.000010	15,064	0.7%

1. Margin of Exposure = DPR NOEL / Dietary Exposure

Chronic Exposure (EX1) Analysis for methidathion
RESIDUE FILE NAME: METHICT2 ANALYSIS DATE: 06-21-2000
NFCS Combined 89-92 DATA
Q_1 = 0.340000
COMMENT 1: Tier 2 Analysis - DPR + PDP monitoring data

TOTAL EXPOSURE BY POPULATION SUBGROUP

POPULATION SUBGROUP	TOTAL EXPOSURE mg/kg body-wt/day	TOTAL EXPOSURE Life-Time Risk (Q_1=0.340000)
U.S. POP - 48 STATES - ALL SEASONS	0.000015	5.20E-06
U.S. POPULATION - SPRING SEASON	0.000014	4.78E-06
U.S. POPULATION - SUMMER SEASON	0.000015	5.23E-06
U.S. POPULATION - AUTUMN SEASON	0.000016	5.49E-06
U.S. POPULATION - WINTER SEASON	0.000015	5.24E-06
NORTHEAST REGION	0.000016	5.51E-06
MIDWEST REGION	0.000016	5.30E-06
SOUTHERN REGION	0.000014	4.89E-06
WESTERN REGION	0.000016	5.27E-06
PACIFIC REGION	0.000015	5.25E-06
HISPANICS	0.000013	4.41E-06
NON-HISPANIC WHITES	0.000016	5.28E-06
NON-HISPANIC BLACKS	0.000015	5.11E-06
NON-HISPANIC OTHER THAN BLACK OR WHITE	0.000017	5.77E-06
ALL INFANTS	0.000035	1.19E-05
NURSING INFANTS (<1 YEAR OLD)	0.000017	5.77E-06
NON-NURSING INFANTS (<1 YEAR OLD)	0.000042	1.44E-05
CHILDREN (1-6 YEARS)	0.000039	1.31E-05
CHILDREN (7-12 YEARS)	0.000026	8.93E-06
FEMALES (13-19 YRS/NOT PREG. OR NURSING)	0.000012	4.03E-06
FEMALES (20+ YEARS/NOT PREG. OR NURSING)	0.000010	3.50E-06
FEMALES (13-50 YEARS)	0.000011	3.68E-06
FEMALES (13+/PREGNANT/NOT NURSING)	0.000013	4.51E-06
FEMALES (13+/NURSING)	0.000019	6.36E-06
MALES (13-19 YEARS)	0.000015	5.10E-06
MALES (20+ YEARS)	0.000011	3.69E-06
SENIORS (55+)	0.000010	3.39E-06

```
Chronic Exposure (EX1) Analysis for methidathion
RESIDUE FILE NAME: METHICT2                          ANALYSIS DATE: 06-21-2000
NFCS Combined 89-92 DATA
Q1* = 0.530000
COMMENT 1: Tier 2 Analysis - DPR + PDP monitoring data
-------------------------------------------------------------------------------
                    TOTAL EXPOSURE BY POPULATION SUBGROUP
-------------------------------------------------------------------------------
```

POPULATION SUBGROUP	TOTAL EXPOSURE mg/kg body-wt/day	Life-Time Risk (Q_1*=0.530000)
U.S. POP - 48 STATES - ALL SEASONS	0.000015	8.10E-06
U.S. POPULATION - SPRING SEASON	0.000014	7.45E-06
U.S. POPULATION - SUMMER SEASON	0.000015	8.16E-06
U.S. POPULATION - AUTUMN SEASON	0.000016	8.56E-06
U.S. POPULATION - WINTER SEASON	0.000015	8.16E-06
NORTHEAST REGION	0.000016	8.59E-06
MIDWEST REGION	0.000016	8.26E-06
SOUTHERN REGION	0.000014	7.62E-06
WESTERN REGION	0.000016	8.22E-06
PACIFIC REGION	0.000015	8.19E-06
HISPANICS	0.000013	6.87E-06
NON-HISPANIC WHITES	0.000016	8.22E-06
NON-HISPANIC BLACKS	0.000015	7.97E-06
NON-HISPANIC OTHER THAN BLACK OR WHITE	0.000017	8.99E-06
ALL INFANTS	0.000035	1.85E-05
NURSING INFANTS (<1 YEAR OLD)	0.000017	9.00E-06
NON-NURSING INFANTS (<1 YEAR OLD)	0.000042	2.25E-05
CHILDREN (1-6 YEARS)	0.000039	2.04E-05
CHILDREN (7-12 YEARS)	0.000026	1.39E-05
FEMALES (13-19 YRS/NOT PREG. OR NURSING)	0.000012	6.28E-06
FEMALES (20+ YEARS/NOT PREG. OR NURSING)	0.000010	5.45E-06
FEMALES (13-50 YEARS)	0.000011	5.74E-06
FEMALES (13+/PREGNANT/NOT NURSING)	0.000013	7.04E-06
FEMALES (13+/NURSING)	0.000019	9.91E-06
MALES (13-19 YEARS)	0.000015	7.95E-06
MALES (20+ YEARS)	0.000011	5.75E-06
SENIORS (55+)	0.000010	5.28E-06

Chronic Exposure (EX1) Analysis for Methidathion
RESIDUE FILE NAME: METHICT3 ANALYSIS DATE: 05-28-1999
NFCS Combined 89-92 DATA
EPA Reference dose (RfD, chronic) = 0.001500 mg/kg body-wt/day
DPR NOEL (Chronic) = 0.150000 mg/kg body-wt/day
COMMENT 1: Tier 3 Analysis - DPR + PDP data with % crop treated

RESIDUE FILE LISTING

TAS CODE	CROP GRP	FOOD NAME	RESIDUE (PPM)	ADJ. FCTRS #1	ADJ. FCTRS #2	SOURCE CODE
20	K	CITRUS CITRON	0.001820	25.00	1.00	PDP-OR
22	K	GRAPEFRUIT-PEELED FRUIT	0.011000	0.10	1.00	DPR
23	K	GRAPEFRUIT-JUICE	0.011000	0.10	1.00	DPR
24	K	KUMQUATS	0.005000	1.00	1.00	DPR
26	K	LEMONS-PEELED FRUIT	0.007000	0.10	1.00	DPR
27	K	LEMONS-PEEL	0.007000	2.50	1.00	DPR
28	K	LEMONS-JUICE	0.007000	0.10	1.00	DPR
30	K	LIMES-PEELED FRUIT	0.006000	0.10	1.00	DPR
31	K	LIMES-PEEL	0.006000	2.50	1.00	DPR
32	K	LIMES-JUICE	0.006000	0.10	1.00	DPR
33	K	ORANGES-JUICE-CONCENTRATE	0.001550	1.00	0.20	PDP
34	K	ORANGES-PEELED FRUIT	0.001820	1.00	0.20	PDP95%
35	K	ORANGES-PEEL	0.001820	25.00	0.20	PDP95%
36	K	ORANGES-JUICE	0.001550	1.00	0.20	PDP
37	K	TANGELOS	0.005000	0.10	1.00	DPR
38	K	TANGERINES	0.015000	0.10	1.00	DPR
39	K	TANGERINES-JUICE	0.015000	0.10	1.00	DPR
40	R	ALMONDS	0.025000	1.00	0.15	1/2TOL
41	R	BRAZIL NUTS	0.025000	1.00	1.00	1/2TOL
42	R	CASHEWS	0.025000	1.00	1.00	1/2TOL
43	R	CHESTNUTS	0.025000	1.00	1.00	1/2TOL
44	R	FILBERTS (HAZELNUTS)	0.025000	1.00	1.00	1/2TOL
45	R	HICKORY NUTS	0.025000	1.00	1.00	1/2TOL
46	R	MACADAMIA NUTS (BUSH NUTS)	0.025000	1.00	1.00	1/2TOL
47	R	PECANS	0.025000	1.00	1.00	1/2TOL
48	R	WALNUTS	0.025000	1.00	0.10	1/2TOL
49	R	BUTTER NUTS	0.025000	1.00	1.00	1/2TOL
50	A	PISTACHIO NUTS	0.025000	1.00	1.00	1/2TOL
51	R	BEECHNUTS	0.025000	1.00	1.00	1/2TOL
52	L	APPLES	0.005000	1.00	0.15	PDP
53	L	APPLES-DRIED	0.005000	8.00	0.15	PDP
54	L	APPLES-JUICE/CIDER	0.001500	1.30	0.15	PDP
55	L	CRABAPPLES	0.005000	1.00	0.15	PDP-AP
56	L	PEARS	0.005000	1.00	0.10	PDP
57	L	PEARS-DRIED	0.005000	6.25	0.10	PDP
58	L	QUINCES	0.005000	1.00	1.00	DPR
59	M	APRICOTS	0.005000	1.00	1.00	DPR
60	M	APRICOTS-DRIED	0.005000	6.00	1.00	DPR
61	M	CHERRIES	0.005000	1.00	1.00	DPR

TAS CODE	CROP GRP	FOOD NAME	RESIDUE (PPM)	ADJ. FCTRS #1	ADJ. FCTRS #2	SOURCE CODE
62	M	CHERRIES-DRIED	0.005000	4.00	1.00	DPR
63	M	CHERRIES-JUICE	0.005000	1.50	1.00	DPR
64	M	NECTARINES	0.005000	1.00	0.35	DPR
65	M	PEACHES	0.001500	1.00	0.35	PDP
66	M	PEACHES-DRIED	0.001500	7.00	0.35	PDP
67	M	PLUMS(DAMSONS)	0.005000	1.00	1.00	DPR
68	M	PLUMS-PRUNES(DRIED)	0.005000	5.00	1.00	DPR
69	M	PLUMS/PRUNE-JUICE	0.005000	1.40	1.00	DPR
80	A	MANGOES	0.025000	1.00	1.00	1/2TOL
82	A	OLIVES	0.025000	1.00	0.10	1/2TOL
97	A	KIWI FRUIT	0.005000	1.00	0.15	DPR
103	A	SUGAR APPLES (SWEETSOP)	0.100000	1.00	1.00	1/2TOL
106	A	CARAMBOLA (STARFRUIT)	0.050000	1.00	1.00	1/2TOL
108	A	LONGAN FRUIT	0.050000	1.00	1.00	1/2TOL
181	A	ARTICHOKES-GLOBE	0.005000	1.00	1.00	DPR
203	B	ARTICHOKES-JERUSALEM	0.005000	1.00	1.00	DPR
246	A	SUNFLOWER-SEEDS-WITH HULLS	0.250000	1.00	1.00	1/2TOL
275	O	SORGHUM (INCLUDING MILO)	0.100000	1.00	1.00	1/2TOL
290	A	COTTONSEED-OIL	0.100000	1.00	0.01	1/2TOL
291	A	COTTONSEED-MEAL	0.100000	1.00	0.01	1/2TOL
294	A	SAFFLOWER-SEED	0.250000	1.00	1.00	1/2TOL
295	A	SAFFLOWER-OIL	0.250000	1.00	1.00	1/2TOL
298	A	SUNFLOWER-OIL	0.250000	1.00	1.00	1/2TOL
300	A	OLIVE OIL	0.025000	1.00	0.10	1/2TOL
318	X	MILK-NONFAT SOLIDS	0.000100	7.87	1.00	REGIST
319	X	MILK-FAT SOLIDS	0.000100	7.87	1.00	REGIST
320	X	MILK SUGAR (LACTOSE)	0.000100	8.13	1.00	REGIST
321	U	BEEF-MEAT BYPRODUCTS	0.000270	1.00	1.00	REGIST
322	U	BEEF(ORGAN MEATS)-OTHER	0.000270	1.00	1.00	REGIST
323	U	BEEF-DRIED	0.000270	1.92	1.00	REGIST
324	U	BEEF(BONELESS)-FAT	0.000030	1.00	1.00	REGIST
325	U	BEEF(ORGAN MEATS)-KIDNEY	0.000180	1.00	1.00	REGIST
326	U	BEEF(ORGAN MEATS)-LIVER	0.000270	1.00	1.00	REGIST
327	U	BEEF(BONELESS)-LEAN (FAT/FREE)	0.000270	1.00	1.00	REGIST
328	U	GOAT-MEAT BYPRODUCTS	0.000270	1.00	1.00	REGIST
329	U	GOAT(ORGAN MEATS)-OTHER	0.000270	1.00	1.00	REGIST
330	U	GOAT(BONELESS)-FAT	0.000030	1.00	1.00	REGIST
331	U	GOAT(ORGAN MEATS)-KIDNEY	0.000180	1.00	1.00	REGIST
332	U	GOAT(ORGAN MEATS)-LIVER	0.000270	1.00	1.00	REGIST
333	U	GOAT(BONELESS)-LEAN (FAT/FREE)	0.000270	1.00	1.00	REGIST
334	U	HORSE	0.000270	1.00	1.00	REGIST
336	U	SHEEP-MEAT BYPRODUCTS	0.000270	1.00	1.00	REGIST
337	U	SHEEP(ORGAN MEATS)-OTHER	0.000270	1.00	1.00	REGIST
338	U	SHEEP(BONELESS)-FAT	0.000030	1.00	1.00	REGIST
339	U	SHEEP(ORGAN MEATS)-KIDNEY	0.000180	1.00	1.00	REGIST
340	U	SHEEP(ORGAN MEATS)-LIVER	0.000270	1.00	1.00	REGIST
341	U	SHEEP(BONELESS)-LEAN (FAT FREE	0.000270	1.00	1.00	REGIST
342	U	PORK-MEAT BYPRODUCTS	0.000140	1.00	1.00	REGIST

TAS CODE	CROP GRP	FOOD NAME	RESIDUE (PPM)	ADJ. FCTRS #1	ADJ. FCTRS #2	SOURCE CODE
343	U	PORK(ORGAN MEATS)-OTHER	0.000140	1.00	1.00	REGIST
344	U	PORK(BONELESS)-FAT	0.000010	1.00	1.00	REGIST
345	U	PORK(ORGAN MEATS)-KIDNEY	0.000090	1.00	1.00	REGIST
346	U	PORK(ORGAN MEATS)-LIVER	0.000140	1.00	1.00	REGIST
347	U	PORK(BONELESS)-LEAN (FAT FREE)	0.000140	1.00	1.00	REGIST
355	V	TURKEY-BYPRODUCTS	0.000090	1.00	1.00	REGIST
356	V	TURKEY-GIBLETS (LIVER)	0.000090	1.00	1.00	REGIST
357	V	TURKEY-(BONELESS)-FAT	0.000030	1.00	1.00	REGIST
358	V	TURKEY-(BONELESS)LEAN/FAT FREE	0.000040	1.00	1.00	REGIST
359	V	TURKEY-UNSPECIFIED	0.000090	1.00	1.00	REGIST
360	V	POULTRY-OTHER-LEAN (FAT FREE)	0.000040	1.00	1.00	REGIST
361	V	POULTRY-OTHER-GIBLETS(LIVER)	0.000090	1.00	1.00	REGIST
362	V	POULTRY-OTHER-FAT	0.000030	1.00	1.00	REGIST
363	X	EGGS-WHOLE	0.000050	1.00	1.00	REGIST
364	X	EGGS-WHITE ONLY	0.000050	1.00	1.00	REGIST
365	X	EGGS-YOLK ONLY	0.000050	1.00	1.00	REGIST
366	V	CHICKEN-BYPRODUCTS	0.000090	1.00	1.00	REGIST
367	V	CHICKEN-GIBLETS(LIVER)	0.000090	1.00	1.00	REGIST
368	V	CHICKEN (BONELESS)-FAT	0.000030	1.00	1.00	REGIST
369	V	CHICKEN(BONELESS)LEAN/FAT FREE	0.000040	1.00	1.00	REGIST
377	L	APPLES-JUICE-CONCENTRATE	0.001500	3.90	0.15	PDP
385	V	CHICKEN-GIBLETS (EXCL. LIVER)	0.000090	1.00	1.00	REGIST
398	X	MILK-BASED WATER	0.000100	1.00	1.00	REGIST
402	M	PEACHES-JUICE	0.001500	1.00	0.35	PDP
404	L	PEARS-NECTAR	0.005000	1.00	0.10	PDP
410	M	APRICOT JUICE OR NECTAR	0.005000	1.00	1.00	DPR
417	A	SUNFLOWER-SEEDS-HULLED	0.250000	1.00	1.00	1/2TOL
420	K	TANGERINES-JUICE-CONCENTRATE	0.015000	0.32	1.00	DPR
424	U	VEAL-(BONELESS)-FAT	0.000030	1.00	1.00	REGIST
425	U	VEAL-(BONELESS)-LEAN (FAT FREE	0.000270	1.00	1.00	REGIST
426	U	VEAL-(ORGAN MEATS)-KIDNEY	0.000180	1.00	1.00	REGIST
427	U	VEAL-(ORGAN MEATS)-LIVER	0.000270	1.00	1.00	REGIST
428	U	VEAL-(ORGAN MEATS)-OTHER	0.000270	1.00	1.00	REGIST
429	U	VEAL-DRIED	0.000270	1.92	1.00	REGIST
430	U	VEAL-MEAT BYPRODUCTS	0.000270	1.00	1.00	REGIST
431	R	WALNUT OIL	0.025000	1.00	0.10	1/2TOL
441	K	GRAPEFRUIT-JUICE-CONCENTRATE	0.011000	0.39	1.00	DPR
442	K	LEMONS-JUICE-CONCENTRATE	0.007000	0.57	1.00	DPR
443	K	LIMES-JUICE-CONCENTRATE	0.006000	0.30	1.00	DPR
448	K	GRAPEFRUIT PEEL	0.014000	2.50	1.00	DPR
449	V	TURKEY-(ORGAN MEATS)-OTHER	0.000080	1.00	1.00	REGIST

Chronic Exposure (EX1) Analysis for Methidathion
RESIDUE FILE NAME: METHICT3 ANALYSIS DATE: 05-28-1999
NFCS Combined 89-92 DATA
EPA Reference dose (RfD, chronic) = 0.001500 mg/kg body-wt/day
DPR NOEL (Chronic) = 0.150000 mg/kg body-wt/day
COMMENT 1: Tier 3 Analysis - DPR + PDP data with % crop treated

TOTAL EXPOSURE BY POPULATION SUBGROUP

POPULATION SUBGROUP	TOTAL EXPOSURE mg/kg body-wt/day	Margin of Exposure 1/	Percent of RfD
U.S. POP - 48 STATES - ALL SEASONS	0.000005	32,741	0.3%
U.S. POPULATION - SPRING SEASON	0.000004	33,544	0.3%
U.S. POPULATION - SUMMER SEASON	0.000005	31,206	0.3%
U.S. POPULATION - AUTUMN SEASON	0.000005	33,279	0.3%
U.S. POPULATION - WINTER SEASON	0.000005	33,192	0.3%
NORTHEAST REGION	0.000005	32,422	0.3%
MIDWEST REGION	0.000005	31,967	0.3%
SOUTHERN REGION	0.000004	35,745	0.3%
WESTERN REGION	0.000005	29,668	0.3%
PACIFIC REGION	0.000005	29,856	0.3%
HISPANICS	0.000005	31,997	0.3%
NON-HISPANIC WHITES	0.000005	32,767	0.3%
NON-HISPANIC BLACKS	0.000004	35,600	0.3%
NON-HISPANIC OTHER THAN BLACK OR WHITE	0.000006	24,580	0.4%
ALL INFANTS	0.000014	10,777	0.9%
NURSING INFANTS (<1 YEAR OLD)	0.000004	41,241	0.2%
NON-NURSING INFANTS (<1 YEAR OLD)	0.000018	8,221	1.2%
CHILDREN (1-6 YEARS)	0.000012	12,558	0.8%
CHILDREN (7-12 YEARS)	0.000008	19,597	0.5%
FEMALES (13-19 YRS/NOT PREG. OR NURSING)	0.000003	48,810	0.2%
FEMALES (20+ YEARS/NOT PREG. OR NURSING)	0.000003	48,703	0.2%
FEMALES (13-50 YEARS)	0.000003	48,916	0.2%
FEMALES (13+/PREGNANT/NOT NURSING)	0.000005	31,834	0.3%
FEMALES (13+/NURSING)	0.000007	21,874	0.5%
MALES (13-19 YEARS)	0.000004	36,336	0.3%
MALES (20+ YEARS)	0.000003	47,343	0.2%
SENIORS (55+)	0.000003	45,952	0.2%

1. Margin of Exposure = DPR NOEL / Dietary Exposure

Chronic Exposure (EX1) Analysis for Methidathion
RESIDUE FILE NAME: METHICT3 ANALYSIS DATE: 06-21-2000
NFCS Combined 89-92 DATA
Q_1 = 0.340000
COMMENT 1: Tier 3 Analysis - DPR + PDP data with % crop treated

TOTAL EXPOSURE BY POPULATION SUBGROUP

POPULATION SUBGROUP	TOTAL EXPOSURE mg/kg body-wt/day	TOTAL EXPOSURE Life-Time Risk (Q_1=0.340000)
U.S. POP - 48 STATES - ALL SEASONS	0.000005	1.56E-06
U.S. POPULATION - SPRING SEASON	0.000004	1.52E-06
U.S. POPULATION - SUMMER SEASON	0.000005	1.63E-06
U.S. POPULATION - AUTUMN SEASON	0.000005	1.53E-06
U.S. POPULATION - WINTER SEASON	0.000005	1.54E-06
NORTHEAST REGION	0.000005	1.57E-06
MIDWEST REGION	0.000005	1.60E-06
SOUTHERN REGION	0.000004	1.43E-06
WESTERN REGION	0.000005	1.72E-06
PACIFIC REGION	0.000005	1.71E-06
HISPANICS	0.000005	1.59E-06
NON-HISPANIC WHITES	0.000005	1.56E-06
NON-HISPANIC BLACKS	0.000004	1.43E-06
NON-HISPANIC OTHER THAN BLACK OR WHITE	0.000006	2.07E-06
ALL INFANTS	0.000014	4.73E-06
NURSING INFANTS (<1 YEAR OLD)	0.000004	1.24E-06
NON-NURSING INFANTS (<1 YEAR OLD)	0.000018	6.20E-06
CHILDREN (1-6 YEARS)	0.000012	4.06E-06
CHILDREN (7-12 YEARS)	0.000008	2.60E-06
FEMALES (13-19 YRS/NOT PREG. OR NURSING)	0.000003	1.04E-06
FEMALES (20+ YEARS/NOT PREG. OR NURSING)	0.000003	1.05E-06
FEMALES (13-50 YEARS)	0.000003	1.04E-06
FEMALES (13+/PREGNANT/NOT NURSING)	0.000005	1.60E-06
FEMALES (13+/NURSING)	0.000007	2.33E-06
MALES (13-19 YEARS)	0.000004	1.40E-06
MALES (20+ YEARS)	0.000003	1.08E-06
SENIORS (55+)	0.000003	1.11E-06

Chronic Exposure (EX1) Analysis for Methidathion
RESIDUE FILE NAME: METHICT3 ANALYSIS DATE: 06-21-2000
NFCS Combined 89-92 DATA
Q_1* = 0.530000
COMMENT 1: Tier 3 Analysis - DPR + PDP data with % crop treated

TOTAL EXPOSURE BY POPULATION SUBGROUP

POPULATION SUBGROUP	TOTAL EXPOSURE mg/kg body-wt/day	TOTAL EXPOSURE Life-Time Risk (Q_1*=0.530000)
U.S. POP - 48 STATES - ALL SEASONS	0.000005	2.43E-06
U.S. POPULATION - SPRING SEASON	0.000004	2.37E-06
U.S. POPULATION - SUMMER SEASON	0.000005	2.55E-06
U.S. POPULATION - AUTUMN SEASON	0.000005	2.39E-06
U.S. POPULATION - WINTER SEASON	0.000005	2.40E-06
NORTHEAST REGION	0.000005	2.45E-06
MIDWEST REGION	0.000005	2.49E-06
SOUTHERN REGION	0.000004	2.22E-06
WESTERN REGION	0.000005	2.68E-06
PACIFIC REGION	0.000005	2.66E-06
HISPANICS	0.000005	2.48E-06
NON-HISPANIC WHITES	0.000005	2.43E-06
NON-HISPANIC BLACKS	0.000004	2.23E-06
NON-HISPANIC OTHER THAN BLACK OR WHITE	0.000006	3.23E-06
ALL INFANTS	0.000014	7.38E-06
NURSING INFANTS (<1 YEAR OLD)	0.000004	1.93E-06
NON-NURSING INFANTS (<1 YEAR OLD)	0.000018	9.67E-06
CHILDREN (1-6 YEARS)	0.000012	6.33E-06
CHILDREN (7-12 YEARS)	0.000008	4.06E-06
FEMALES (13-19 YRS/NOT PREG. OR NURSING)	0.000003	1.63E-06
FEMALES (20+ YEARS/NOT PREG. OR NURSING)	0.000003	1.63E-06
FEMALES (13-50 YEARS)	0.000003	1.63E-06
FEMALES (13+/PREGNANT/NOT NURSING)	0.000005	2.50E-06
FEMALES (13+/NURSING)	0.000007	3.63E-06
MALES (13-19 YEARS)	0.000004	2.19E-06
MALES (20+ YEARS)	0.000003	1.68E-06
SENIORS (55+)	0.000003	1.73E-06

Chronic Exposure (EX1) Analysis for Methidathion
RESIDUE FILE NAME: METHICT4 ANALYSIS DATE: 05-28-1999
NFCS Combined 89-92 DATA
EPA Reference dose (RfD, chronic) = 0.001500 mg/kg body-wt/day
DPR NOEL (Chronic) = 0.150000 mg/kg body-wt/day
COMMENT 1: Tier 4 Analysis - Tier 3 with secondary residues removed

RESIDUE FILE LISTING

TAS CODE	CROP GRP	FOOD NAME	RESIDUE (PPM)	ADJ. FCTRS #1	ADJ. FCTRS #2	SOURCE CODE
20	K	CITRUS CITRON	0.001820	25.00	1.00	PDP-OR
22	K	GRAPEFRUIT-PEELED FRUIT	0.011000	0.10	1.00	DPR
23	K	GRAPEFRUIT-JUICE	0.011000	0.10	1.00	DPR
24	K	KUMQUATS	0.005000	1.00	1.00	DPR
26	K	LEMONS-PEELED FRUIT	0.007000	0.10	1.00	DPR
27	K	LEMONS-PEEL	0.007000	2.50	1.00	DPR
28	K	LEMONS-JUICE	0.007000	0.10	1.00	DPR
30	K	LIMES-PEELED FRUIT	0.006000	0.10	1.00	DPR
31	K	LIMES-PEEL	0.006000	2.50	1.00	DPR
32	K	LIMES-JUICE	0.006000	0.10	1.00	DPR
33	K	ORANGES-JUICE-CONCENTRATE	0.000350	1.00	1.00	PDP
34	K	ORANGES-PEELED FRUIT	0.000618	1.00	1.00	PDP95%
35	K	ORANGES-PEEL	0.000618	25.00	1.00	PDP95%
36	K	ORANGES-JUICE	0.000350	1.00	1.00	PDP
37	K	TANGELOS	0.005000	0.10	1.00	DPR
38	K	TANGERINES	0.015000	0.10	1.00	DPR
39	K	TANGERINES-JUICE	0.015000	0.10	1.00	DPR
40	R	ALMONDS	0.025000	1.00	0.15	1/2TOL
41	R	BRAZIL NUTS	0.025000	1.00	1.00	1/2TOL
42	R	CASHEWS	0.025000	1.00	1.00	1/2TOL
43	R	CHESTNUTS	0.025000	1.00	1.00	1/2TOL
44	R	FILBERTS (HAZELNUTS)	0.025000	1.00	1.00	1/2TOL
45	R	HICKORY NUTS	0.025000	1.00	1.00	1/2TOL
46	R	MACADAMIA NUTS (BUSH NUTS)	0.025000	1.00	1.00	1/2TOL
47	R	PECANS	0.025000	1.00	1.00	1/2TOL
48	R	WALNUTS	0.025000	1.00	0.10	1/2TOL
49	R	BUTTER NUTS	0.025000	1.00	1.00	1/2TOL
50	A	PISTACHIO NUTS	0.025000	1.00	1.00	1/2TOL
51	R	BEECHNUTS	0.025000	1.00	1.00	1/2TOL
52	L	APPLES	0.005000	1.00	0.15	PDP
53	L	APPLES-DRIED	0.005000	8.00	0.15	PDP
54	L	APPLES-JUICE/CIDER	0.001500	1.30	0.15	PDP
55	L	CRABAPPLES	0.005000	1.00	0.15	PDP-AP
56	L	PEARS	0.005000	1.00	0.10	PDP
57	L	PEARS-DRIED	0.005000	6.25	0.10	PDP
58	L	QUINCES	0.005000	1.00	1.00	DPR
59	M	APRICOTS	0.005000	1.00	1.00	DPR
60	M	APRICOTS-DRIED	0.005000	6.00	1.00	DPR
61	M	CHERRIES	0.005000	1.00	1.00	DPR

TAS CODE	CROP GRP	FOOD NAME	RESIDUE (PPM)	ADJ. FCTRS #1	ADJ. FCTRS #2	SOURCE CODE
62	M	CHERRIES-DRIED	0.005000	4.00	1.00	DPR
63	M	CHERRIES-JUICE	0.005000	1.50	1.00	DPR
64	M	NECTARINES	0.005000	1.00	0.35	DPR
65	M	PEACHES	0.001500	1.00	0.35	PDP
66	M	PEACHES-DRIED	0.001500	7.00	0.35	PDP
67	M	PLUMS(DAMSONS)	0.005000	1.00	1.00	DPR
68	M	PLUMS-PRUNES(DRIED)	0.005000	5.00	1.00	DPR
69	M	PLUMS/PRUNE-JUICE	0.005000	1.40	1.00	DPR
80	A	MANGOES	0.025000	1.00	1.00	1/2TOL
82	A	OLIVES	0.025000	1.00	0.10	1/2TOL
97	A	KIWI FRUIT	0.005000	1.00	0.15	DPR
103	A	SUGAR APPLES (SWEETSOP)	0.100000	1.00	1.00	1/2TOL
106	A	CARAMBOLA (STARFRUIT)	0.050000	1.00	1.00	1/2TOL
108	A	LONGAN FRUIT	0.050000	1.00	1.00	1/2TOL
181	A	ARTICHOKES-GLOBE	0.005000	1.00	1.00	DPR
203	B	ARTICHOKES-JERUSALEM	0.005000	1.00	1.00	DPR
246	A	SUNFLOWER-SEEDS-WITH HULLS	0.250000	1.00	1.00	1/2TOL
275	O	SORGHUM (INCLUDING MILO)	0.100000	1.00	1.00	1/2TOL
290	A	COTTONSEED-OIL	0.100000	1.00	0.01	1/2TOL
291	A	COTTONSEED-MEAL	0.100000	1.00	0.01	1/2TOL
294	A	SAFFLOWER-SEED	0.250000	1.00	1.00	1/2TOL
295	A	SAFFLOWER-OIL	0.250000	1.00	1.00	1/2TOL
298	A	SUNFLOWER-OIL	0.250000	1.00	1.00	1/2TOL
300	A	OLIVE OIL	0.025000	1.00	0.10	1/2TOL
377	L	APPLES-JUICE-CONCENTRATE	0.001500	3.90	0.15	PDP
402	M	PEACHES-JUICE	0.001500	1.00	0.35	PDP
404	L	PEARS-NECTAR	0.005000	1.00	0.10	PDP
410	M	APRICOT JUICE OR NECTAR	0.005000	1.00	1.00	DPR
417	A	SUNFLOWER-SEEDS-HULLED	0.250000	1.00	1.00	1/2TOL
420	K	TANGERINES-JUICE-CONCENTRATE	0.015000	0.32	1.00	DPR
431	R	WALNUT OIL	0.025000	1.00	0.10	1/2TOL
441	K	GRAPEFRUIT-JUICE-CONCENTRATE	0.011000	0.39	1.00	DPR
442	K	LEMONS-JUICE-CONCENTRATE	0.007000	0.57	1.00	DPR
443	K	LIMES-JUICE-CONCENTRATE	0.006000	0.30	1.00	DPR
448	K	GRAPEFRUIT PEEL	0.014000	2.50	1.00	DPR

Chronic Exposure (EX1) Analysis for Methidathion
RESIDUE FILE NAME: METHICT4 ANALYSIS DATE: 05-28-1999
NFCS Combined 89-92 DATA
EPA Reference dose (RfD, chronic) = 0.001500 mg/kg body-wt/day
DPR NOEL (Chronic) = 0.150000 mg/kg body-wt/day
COMMENT 1: Tier 4 Analysis - Tier 3 with secondary residues removed

TOTAL EXPOSURE BY POPULATION SUBGROUP

POPULATION SUBGROUP	TOTAL EXPOSURE mg/kg body-wt/day	Margin of Exposure 1/	Percent of RfD
U.S. POP - 48 STATES - ALL SEASONS	0.000003	54,512	0.2%
U.S. POPULATION - SPRING SEASON	0.000003	57,163	0.2%
U.S. POPULATION - SUMMER SEASON	0.000003	49,772	0.2%
U.S. POPULATION - AUTUMN SEASON	0.000003	57,508	0.2%
U.S. POPULATION - WINTER SEASON	0.000003	54,774	0.2%
NORTHEAST REGION	0.000003	53,260	0.2%
MIDWEST REGION	0.000003	57,133	0.2%
SOUTHERN REGION	0.000003	59,484	0.2%
WESTERN REGION	0.000003	46,468	0.2%
PACIFIC REGION	0.000003	46,515	0.2%
HISPANICS	0.000003	55,909	0.2%
NON-HISPANIC WHITES	0.000003	54,631	0.2%
NON-HISPANIC BLACKS	0.000003	59,001	0.2%
NON-HISPANIC OTHER THAN BLACK OR WHITE	0.000004	35,960	0.3%
ALL INFANTS	0.000008	19,523	0.5%
NURSING INFANTS (<1 YEAR OLD)	0.000002	62,731	0.2%
NON-NURSING INFANTS (<1 YEAR OLD)	0.000010	15,134	0.7%
CHILDREN (1-6 YEARS)	0.000006	24,536	0.4%
CHILDREN (7-12 YEARS)	0.000005	33,321	0.3%
FEMALES (13-19 YRS/NOT PREG. OR NURSING)	0.000002	96,320	0.1%
FEMALES (20+ YEARS/NOT PREG. OR NURSING)	0.000002	71,775	0.1%
FEMALES (13-50 YEARS)	0.000002	76,580	0.1%
FEMALES (13+/PREGNANT/NOT NURSING)	0.000003	48,631	0.2%
FEMALES (13+/NURSING)	0.000005	27,880	0.4%
MALES (13-19 YEARS)	0.000002	68,454	0.1%
MALES (20+ YEARS)	0.000002	72,012	0.1%
SENIORS (55+)	0.000002	65,242	0.2%

1. Margin of Exposure = DPR NOEL / Dietary Exposure

Chronic Exposure (EX1) Analysis for Methidathion
RESIDUE FILE NAME: METHICT4 ANALYSIS DATE: 06-21-2000
NFCS Combined 89-92 DATA
Q_1 = 0.340000
COMMENT 1: Tier 4 Analysis - Tier 3 with secondary residues removed

TOTAL EXPOSURE BY POPULATION SUBGROUP

POPULATION SUBGROUP	TOTAL EXPOSURE mg/kg body-wt/day	Life-Time Risk (Q_1=0.340000)
U.S. POP - 48 STATES - ALL SEASONS	0.000003	9.36E-07
U.S. POPULATION - SPRING SEASON	0.000003	8.92E-07
U.S. POPULATION - SUMMER SEASON	0.000003	1.02E-06
U.S. POPULATION - AUTUMN SEASON	0.000003	8.87E-07
U.S. POPULATION - WINTER SEASON	0.000003	9.31E-07
NORTHEAST REGION	0.000003	9.58E-07
MIDWEST REGION	0.000003	8.93E-07
SOUTHERN REGION	0.000003	8.57E-07
WESTERN REGION	0.000003	1.10E-06
PACIFIC REGION	0.000003	1.10E-06
HISPANICS	0.000003	9.12E-07
NON-HISPANIC WHITES	0.000003	9.34E-07
NON-HISPANIC BLACKS	0.000003	8.64E-07
NON-HISPANIC OTHER THAN BLACK OR WHITE	0.000004	1.42E-06
ALL INFANTS	0.000008	2.61E-06
NURSING INFANTS (<1 YEAR OLD)	0.000002	8.13E-07
NON-NURSING INFANTS (<1 YEAR OLD)	0.000010	3.37E-06
CHILDREN (1-6 YEARS)	0.000006	2.08E-06
CHILDREN (7-12 YEARS)	0.000005	1.53E-06
FEMALES (13-19 YRS/NOT PREG. OR NURSING)	0.000002	5.29E-07
FEMALES (20+ YEARS/NOT PREG. OR NURSING)	0.000002	7.11E-07
FEMALES (13-50 YEARS)	0.000002	6.66E-07
FEMALES (13+/PREGNANT/NOT NURSING)	0.000003	1.05E-06
FEMALES (13+/NURSING)	0.000005	1.83E-06
MALES (13-19 YEARS)	0.000002	7.45E-07
MALES (20+ YEARS)	0.000002	7.08E-07
SENIORS (55+)	0.000002	7.82E-07

Chronic Exposure (EX1) Analysis for Methidathion
RESIDUE FILE NAME: METHICT4 ANALYSIS DATE: 06-21-2000
NFCS Combined 89-92 DATA
Q_1^* = 0.530000
COMMENT 1: Tier 4 Analysis - Tier 3 with secondary residues removed

TOTAL EXPOSURE BY POPULATION SUBGROUP

POPULATION SUBGROUP	TOTAL EXPOSURE mg/kg body-wt/day	TOTAL EXPOSURE Life-Time Risk (Q_1^*=0.530000)
U.S. POP - 48 STATES - ALL SEASONS	0.000003	1.46E-06
U.S. POPULATION - SPRING SEASON	0.000003	1.39E-06
U.S. POPULATION - SUMMER SEASON	0.000003	1.60E-06
U.S. POPULATION - AUTUMN SEASON	0.000003	1.38E-06
U.S. POPULATION - WINTER SEASON	0.000003	1.45E-06
NORTHEAST REGION	0.000003	1.49E-06
MIDWEST REGION	0.000003	1.39E-06
SOUTHERN REGION	0.000003	1.34E-06
WESTERN REGION	0.000003	1.71E-06
PACIFIC REGION	0.000003	1.71E-06
HISPANICS	0.000003	1.42E-06
NON-HISPANIC WHITES	0.000003	1.46E-06
NON-HISPANIC BLACKS	0.000003	1.35E-06
NON-HISPANIC OTHER THAN BLACK OR WHITE	0.000004	2.21E-06
ALL INFANTS	0.000008	4.07E-06
NURSING INFANTS (<1 YEAR OLD)	0.000002	1.27E-06
NON-NURSING INFANTS (<1 YEAR OLD)	0.000010	5.25E-06
CHILDREN (1-6 YEARS)	0.000006	3.24E-06
CHILDREN (7-12 YEARS)	0.000005	2.39E-06
FEMALES (13-19 YRS/NOT PREG. OR NURSING)	0.000002	8.25E-07
FEMALES (20+ YEARS/NOT PREG. OR NURSING)	0.000002	1.11E-06
FEMALES (13-50 YEARS)	0.000002	1.04E-06
FEMALES (13+/PREGNANT/NOT NURSING)	0.000003	1.63E-06
FEMALES (13+/NURSING)	0.000005	2.85E-06
MALES (13-19 YEARS)	0.000002	1.16E-06
MALES (20+ YEARS)	0.000002	1.10E-06
SENIORS (55+)	0.000002	1.22E-06

```
ACUTE EXPOSURE (EX4) ANALYSIS FOR METHIDATHION
Residue file name: METHWATA                         Analysis date: 06-14-2000
1989-92 DATA   Adjustment factor #2 NOT used
DPR NOEL (Acute) =   0.300000 mg/kg body-wt/day
COMMENT 1: Surface Drinking Water
===============================================================================
                         RESIDUE FILE LISTING
-------------------------------------------------------------------------------
 TAS  CROP                                        RESIDUE  ADJ. FCTRS   SOURCE
CODE   GRP           FOOD NAME                     (PPM)     #1    #2    CODE
----  ---- ------------------------------------- ---------- ----- -----  ------
432     A  WATER-BOTTLED                         no consumption in survey
433     A  WATER-TAP                               0.000654  1.00  1.00
434     A  WATER-COMMERCIAL PROCESSING             0.000654  1.00  1.00
435     A  WATER-NON-FOOD BASED                    0.000654  1.00  1.00
```

ACUTE EXPOSURE (EX4) ANALYSIS FOR METHIDATHION
Residue file name: METHWATA Analysis date: 06-14-2000
1989-92 DATA Adjustment factor #2 NOT used
DPR NOEL (Acute) = 0.300000 mg/kg body-wt/day
Initial estimate of user-days as % of person-days in survey = 100.00%
COMMENT 1: Surface Drinking Water

U.S. POP - ALL SEASONS

Daily Exposure Analysis 1/ (mg/kg body-weight/day)

	per Capita	per User
Mean	0.000019	0.000019
Standard Deviation	0.000014	0.000014
Standard Error	0.000000	0.000000

Percent of Person-Days that are User-Days = 99.83%

ESTIMATED PERCENTILE OF USER-DAYS LESS THAN/EQUAL TO CALCULATED EXPOSURE
in mg/kg body-wt/day and corresponding Margin of Exposure (MOE)

PERCENTILE	EXPOSURE	MOE 2/	PERCENTILE	EXPOSURE	MOE
10.00	0.000008	39,466	90.00	0.000032	9,297
20.00	0.000010	30,106	95.00	0.000042	7,196
30.00	0.000012	25,020	97.50	0.000053	5,615
40.00	0.000014	21,410	99.00	0.000074	4,078
50.00	0.000016	18,640	99.50	0.000094	3,189
60.00	0.000018	16,300	99.75	0.000115	2,616
70.00	0.000021	14,098	99.90	0.000150	1,994
80.00	0.000025	11,824			

ESTIMATED PERCENTILE OF PER-CAPITA DAYS LESS THAN/EQUAL TO CALCULATED EXPOSURE
in mg/kg body-wt/day and corresponding Margin of Exposure (MOE)

PERCENTILE	EXPOSURE	MOE 2/	PERCENTILE	EXPOSURE	MOE
10.00	0.000007	40,076	90.00	0.000032	9,300
20.00	0.000010	30,203	95.00	0.000042	7,199
30.00	0.000012	25,070	97.50	0.000053	5,617
40.00	0.000014	21,442	99.00	0.000074	4,080
50.00	0.000016	18,660	99.50	0.000094	3,190
60.00	0.000018	16,314	99.75	0.000115	2,617
70.00	0.000021	14,108	99.90	0.000150	1,994
80.00	0.000025	11,830			

1/ Analysis based on all participant-days in NFCS 1989-92 survey.
2/ Margin of Exposure = NOEL/ Dietary Exposure.

ACUTE EXPOSURE (EX4) ANALYSIS FOR METHIDATHION
Residue file name: METHWATA Analysis date: 06-14-2000
1989-92 DATA Adjustment factor #2 NOT used
DPR NOEL (Acute) = 0.300000 mg/kg body-wt/day

WESTERN REGION

	Daily Exposure Analysis (mg/kg body-weight/day) per Capita	per User
Mean	0.000020	0.000020
Standard Deviation	0.000014	0.000014
Standard Error	0.000000	0.000000

Percent of Person-Days that are User-Days = 99.68%

ESTIMATED PERCENTILE OF USER-DAYS LESS THAN/EQUAL TO CALCULATED EXPOSURE
in mg/kg body-wt/day and corresponding Margin of Exposure (MOE)

PERCENTILE	EXPOSURE	MOE 2/	PERCENTILE	EXPOSURE	MOE
10.00	0.000007	40,668	90.00	0.000035	8,682
20.00	0.000010	30,550	95.00	0.000046	6,511
30.00	0.000012	25,027	97.50	0.000060	5,006
40.00	0.000014	21,482	99.00	0.000079	3,790
50.00	0.000016	18,624	99.50	0.000101	2,972
60.00	0.000019	15,994	99.75	0.000108	2,768
70.00	0.000022	13,664	99.90	0.000113	2,658
80.00	0.000026	11,338			

ESTIMATED PERCENTILE OF PER-CAPITA DAYS LESS THAN/EQUAL TO CALCULATED EXPOSURE
in mg/kg body-wt/day and corresponding Margin of Exposure (MOE)

PERCENTILE	EXPOSURE	MOE 2/	PERCENTILE	EXPOSURE	MOE
10.00	0.000007	41,863	90.00	0.000035	8,689
20.00	0.000010	30,744	95.00	0.000046	6,516
30.00	0.000012	25,128	97.50	0.000060	5,009
40.00	0.000014	21,540	99.00	0.000079	3,792
50.00	0.000016	18,664	99.50	0.000101	2,974
60.00	0.000019	16,023	99.75	0.000108	2,768
70.00	0.000022	13,683	99.90	0.000113	2,658
80.00	0.000026	11,350			

ACUTE EXPOSURE (EX4) ANALYSIS FOR METHIDATHION
Residue file name: METHWATA Analysis date: 06-14-2000
1989-92 DATA Adjustment factor #2 NOT used
DPR NOEL (Acute) = 0.300000 mg/kg body-wt/day

NURSING INFANTS (<1 YEAR)

	Daily Exposure Analysis (mg/kg body-weight/day) per Capita	per User
Mean	0.000016	0.000025
Standard Deviation	0.000020	0.000019
Standard Error	0.000002	0.000002

Percent of Person-Days that are User-Days = 63.01%

ESTIMATED PERCENTILE OF USER-DAYS LESS THAN/EQUAL TO CALCULATED EXPOSURE
in mg/kg body-wt/day and corresponding Margin of Exposure (MOE)

PERCENTILE	EXPOSURE	MOE 2/	PERCENTILE	EXPOSURE	MOE
10.00	0.000006	47,812	90.00	0.000056	5,364
20.00	0.000012	24,346	95.00	0.000063	4,780
30.00	0.000013	23,031	97.50	0.000070	4,304
40.00	0.000014	21,851	99.00	0.000080	3,737
50.00	0.000017	17,808	99.50	0.000082	3,638
60.00	0.000020	14,876	99.75	0.000084	3,590
70.00	0.000034	8,935	99.90	0.000084	3,562
80.00	0.000045	6,659			

ESTIMATED PERCENTILE OF PER-CAPITA DAYS LESS THAN/EQUAL TO CALCULATED EXPOSURE
in mg/kg body-wt/day and corresponding Margin of Exposure (MOE)

PERCENTILE	EXPOSURE	MOE 2/	PERCENTILE	EXPOSURE	MOE
10.00	0.000000	>1,000,000	90.00	0.000050	6,055
20.00	0.000000	>1,000,000	95.00	0.000059	5,106
30.00	0.000000	>1,000,000	97.50	0.000066	4,571
40.00	0.000003	100,106	99.00	0.000076	3,940
50.00	0.000012	24,257	99.50	0.000081	3,695
60.00	0.000013	22,248	99.75	0.000083	3,618
70.00	0.000018	17,008	99.90	0.000084	3,573
80.00	0.000031	9,603			

ACUTE EXPOSURE (EX4) ANALYSIS FOR METHIDATHION
Residue file name: METHWATA Analysis date: 06-14-2000
1989-92 DATA Adjustment factor #2 NOT used
DPR NOEL (Acute) = 0.300000 mg/kg body-wt/day

NON-NURSING INFANTS (<1)

	Daily Exposure Analysis (mg/kg body-weight/day) per Capita	per User
Mean	0.000087	0.000087
Standard Deviation	0.000045	0.000045
Standard Error	0.000002	0.000002

Percent of Person-Days that are User-Days =100.00%

ESTIMATED PERCENTILE OF USER-DAYS LESS THAN/EQUAL TO CALCULATED EXPOSURE
in mg/kg body-wt/day and corresponding Margin of Exposure (MOE)

PERCENTILE	EXPOSURE	MOE 2/	PERCENTILE	EXPOSURE	MOE
10.00	0.000033	9,181	90.00	0.000144	2,088
20.00	0.000051	5,935	95.00	0.000181	1,655
30.00	0.000063	4,781	97.50	0.000191	1,573
40.00	0.000070	4,283	99.00	0.000196	1,528
50.00	0.000080	3,728	99.50	0.000231	1,299
60.00	0.000097	3,094	99.75	0.000257	1,165
70.00	0.000105	2,849	99.90	0.000288	1,042
80.00	0.000117	2,574			

ESTIMATED PERCENTILE OF PER-CAPITA DAYS LESS THAN/EQUAL TO CALCULATED EXPOSURE
in mg/kg body-wt/day and corresponding Margin of Exposure (MOE)

PERCENTILE	EXPOSURE	MOE 2/	PERCENTILE	EXPOSURE	MOE
10.00	0.000033	9,181	90.00	0.000144	2,088
20.00	0.000051	5,935	95.00	0.000181	1,655
30.00	0.000063	4,781	97.50	0.000191	1,573
40.00	0.000070	4,283	99.00	0.000196	1,528
50.00	0.000080	3,728	99.50	0.000231	1,299
60.00	0.000097	3,094	99.75	0.000257	1,165
70.00	0.000105	2,849	99.90	0.000288	1,042
80.00	0.000117	2,574			

ACUTE EXPOSURE (EX4) ANALYSIS FOR METHIDATHION
Residue file name: METHWATA Analysis date: 06-14-2000
1989-92 DATA Adjustment factor #2 NOT used
DPR NOEL (Acute) = 0.300000 mg/kg body-wt/day

FEMALES (13+/PREG/NOT NSG)

	Daily Exposure Analysis (mg/kg body-weight/day) per Capita	per User
Mean	0.000015	0.000015
Standard Deviation	0.000009	0.000009
Standard Error	0.000000	0.000000

Percent of Person-Days that are User-Days =100.00%

ESTIMATED PERCENTILE OF USER-DAYS LESS THAN/EQUAL TO CALCULATED EXPOSURE
in mg/kg body-wt/day and corresponding Margin of Exposure (MOE)

PERCENTILE	EXPOSURE	MOE 2/	PERCENTILE	EXPOSURE	MOE
10.00	0.000005	58,615	90.00	0.000027	11,302
20.00	0.000008	38,252	95.00	0.000033	9,152
30.00	0.000010	29,435	97.50	0.000035	8,555
40.00	0.000012	25,108	99.00	0.000044	6,861
50.00	0.000014	21,716	99.50	0.000046	6,555
60.00	0.000016	18,904	99.75	0.000047	6,412
70.00	0.000018	16,469	99.90	0.000048	6,232
80.00	0.000021	14,085			

ESTIMATED PERCENTILE OF PER-CAPITA DAYS LESS THAN/EQUAL TO CALCULATED EXPOSURE
in mg/kg body-wt/day and corresponding Margin of Exposure (MOE)

PERCENTILE	EXPOSURE	MOE 2/	PERCENTILE	EXPOSURE	MOE
10.00	0.000005	58,615	90.00	0.000027	11,302
20.00	0.000008	38,252	95.00	0.000033	9,152
30.00	0.000010	29,435	97.50	0.000035	8,555
40.00	0.000012	25,108	99.00	0.000044	6,861
50.00	0.000014	21,716	99.50	0.000046	6,555
60.00	0.000016	18,904	99.75	0.000047	6,412
70.00	0.000018	16,469	99.90	0.000048	6,232
80.00	0.000021	14,085			

ACUTE EXPOSURE (EX4) ANALYSIS FOR METHIDATHION
Residue file name: METHWATA Analysis date: 06-14-2000
1989-92 DATA Adjustment factor #2 NOT used
DPR NOEL (Acute) = 0.300000 mg/kg body-wt/day

FEMALES (13+/NURSING)

	Daily Exposure Analysis (mg/kg body-weight/day) per Capita	per User
Mean	0.000020	0.000020
Standard Deviation	0.000010	0.000010
Standard Error	0.000001	0.000001

Percent of Person-Days that are User-Days =100.00%

ESTIMATED PERCENTILE OF USER-DAYS LESS THAN/EQUAL TO CALCULATED EXPOSURE
in mg/kg body-wt/day and corresponding Margin of Exposure (MOE)

PERCENTILE	EXPOSURE	MOE 2/	PERCENTILE	EXPOSURE	MOE
10.00	0.000009	33,650	90.00	0.000030	9,959
20.00	0.000012	24,974	95.00	0.000037	8,165
30.00	0.000013	22,526	97.50	0.000047	6,381
40.00	0.000015	19,480	99.00	0.000060	5,006
50.00	0.000018	16,884	99.50	0.000067	4,501
60.00	0.000021	14,235	99.75	0.000068	4,393
70.00	0.000023	12,901	99.90	0.000069	4,331
80.00	0.000026	11,637			

ESTIMATED PERCENTILE OF PER-CAPITA DAYS LESS THAN/EQUAL TO CALCULATED EXPOSURE
in mg/kg body-wt/day and corresponding Margin of Exposure (MOE)

PERCENTILE	EXPOSURE	MOE 2/	PERCENTILE	EXPOSURE	MOE
10.00	0.000009	33,650	90.00	0.000030	9,959
20.00	0.000012	24,974	95.00	0.000037	8,165
30.00	0.000013	22,526	97.50	0.000047	6,381
40.00	0.000015	19,480	99.00	0.000060	5,006
50.00	0.000018	16,884	99.50	0.000067	4,501
60.00	0.000021	14,235	99.75	0.000068	4,393
70.00	0.000023	12,901	99.90	0.000069	4,331
80.00	0.000026	11,637			

ACUTE EXPOSURE (EX4) ANALYSIS FOR METHIDATHION
Residue file name: METHWATA Analysis date: 06-14-2000
1989-92 DATA Adjustment factor #2 NOT used
DPR NOEL (Acute) = 0.300000 mg/kg body-wt/day

CHILDREN (1-6 YEARS)

Daily Exposure Analysis (mg/kg body-weight/day)

	per Capita	per User
Mean	0.000030	0.000030
Standard Deviation	0.000018	0.000018
Standard Error	0.000000	0.000000

Percent of Person-Days that are User-Days = 99.92%

ESTIMATED PERCENTILE OF USER-DAYS LESS THAN/EQUAL TO CALCULATED EXPOSURE
in mg/kg body-wt/day and corresponding Margin of Exposure (MOE)

PERCENTILE	EXPOSURE	MOE 2/	PERCENTILE	EXPOSURE	MOE
10.00	0.000011	27,623	90.00	0.000053	5,706
20.00	0.000016	18,965	95.00	0.000062	4,876
30.00	0.000019	15,452	97.50	0.000072	4,167
40.00	0.000023	13,063	99.00	0.000084	3,553
50.00	0.000027	11,217	99.50	0.000098	3,077
60.00	0.000030	9,888	99.75	0.000110	2,739
70.00	0.000035	8,553	99.90	0.000126	2,382
80.00	0.000042	7,151			

ESTIMATED PERCENTILE OF PER-CAPITA DAYS LESS THAN/EQUAL TO CALCULATED EXPOSURE
in mg/kg body-wt/day and corresponding Margin of Exposure (MOE)

PERCENTILE	EXPOSURE	MOE 2/	PERCENTILE	EXPOSURE	MOE
10.00	0.000011	27,812	90.00	0.000053	5,707
20.00	0.000016	19,001	95.00	0.000062	4,876
30.00	0.000019	15,468	97.50	0.000072	4,167
40.00	0.000023	13,072	99.00	0.000084	3,553
50.00	0.000027	11,223	99.50	0.000097	3,077
60.00	0.000030	9,891	99.75	0.000110	2,740
70.00	0.000035	8,556	99.90	0.000126	2,382
80.00	0.000042	7,153			

ACUTE EXPOSURE (EX4) ANALYSIS FOR METHIDATHION
Residue file name: METHWATA Analysis date: 06-14-2000
1989-92 DATA Adjustment factor #2 NOT used
DPR NOEL (Acute) = 0.300000 mg/kg body-wt/day

CHILDREN (7-12 YEARS)

	Daily Exposure Analysis (mg/kg body-weight/day) per Capita	per User
Mean	0.000020	0.000020
Standard Deviation	0.000011	0.000011
Standard Error	0.000000	0.000000

Percent of Person-Days that are User-Days = 99.98%

ESTIMATED PERCENTILE OF USER-DAYS LESS THAN/EQUAL TO CALCULATED EXPOSURE
in mg/kg body-wt/day and corresponding Margin of Exposure (MOE)

PERCENTILE	EXPOSURE	MOE 2/	PERCENTILE	EXPOSURE	MOE
10.00	0.000008	36,926	90.00	0.000034	8,780
20.00	0.000011	27,657	95.00	0.000042	7,213
30.00	0.000013	23,102	97.50	0.000050	6,028
40.00	0.000015	19,786	99.00	0.000058	5,133
50.00	0.000017	17,146	99.50	0.000065	4,610
60.00	0.000020	14,986	99.75	0.000070	4,294
70.00	0.000023	12,992	99.90	0.000075	3,994
80.00	0.000027	11,054			

ESTIMATED PERCENTILE OF PER-CAPITA DAYS LESS THAN/EQUAL TO CALCULATED EXPOSURE
in mg/kg body-wt/day and corresponding Margin of Exposure (MOE)

PERCENTILE	EXPOSURE	MOE 2/	PERCENTILE	EXPOSURE	MOE
10.00	0.000008	36,999	90.00	0.000034	8,780
20.00	0.000011	27,669	95.00	0.000042	7,213
30.00	0.000013	23,108	97.50	0.000050	6,028
40.00	0.000015	19,790	99.00	0.000058	5,133
50.00	0.000017	17,148	99.50	0.000065	4,610
60.00	0.000020	14,988	99.75	0.000070	4,294
70.00	0.000023	12,993	99.90	0.000075	3,994
80.00	0.000027	11,055			

ACUTE EXPOSURE (EX4) ANALYSIS FOR METHIDATHION
Residue file name: METHWATA Analysis date: 06-14-2000
1989-92 DATA Adjustment factor #2 NOT used
DPR NOEL (Acute) = 0.300000 mg/kg body-wt/day

MALES (13-19 YEARS)

	Daily Exposure Analysis (mg/kg body-weight/day) per Capita	per User
Mean	0.000016	0.000016
Standard Deviation	0.000011	0.000011
Standard Error	0.000000	0.000000

Percent of Person-Days that are User-Days =100.00%

ESTIMATED PERCENTILE OF USER-DAYS LESS THAN/EQUAL TO CALCULATED EXPOSURE
in mg/kg body-wt/day and corresponding Margin of Exposure (MOE)

PERCENTILE	EXPOSURE	MOE 2/	PERCENTILE	EXPOSURE	MOE
10.00	0.000005	60,196	90.00	0.000026	11,454
20.00	0.000008	38,203	95.00	0.000033	9,090
30.00	0.000010	29,911	97.50	0.000045	6,630
40.00	0.000012	24,822	99.00	0.000062	4,868
50.00	0.000014	21,038	99.50	0.000078	3,854
60.00	0.000017	18,127	99.75	0.000083	3,624
70.00	0.000019	15,963	99.90	0.000085	3,535
80.00	0.000022	13,939			

ESTIMATED PERCENTILE OF PER-CAPITA DAYS LESS THAN/EQUAL TO CALCULATED EXPOSURE
in mg/kg body-wt/day and corresponding Margin of Exposure (MOE)

PERCENTILE	EXPOSURE	MOE 2/	PERCENTILE	EXPOSURE	MOE
10.00	0.000005	60,196	90.00	0.000026	11,454
20.00	0.000008	38,203	95.00	0.000033	9,090
30.00	0.000010	29,911	97.50	0.000045	6,630
40.00	0.000012	24,822	99.00	0.000062	4,868
50.00	0.000014	21,038	99.50	0.000078	3,854
60.00	0.000017	18,127	99.75	0.000083	3,624
70.00	0.000019	15,963	99.90	0.000085	3,535
80.00	0.000022	13,939			

ACUTE EXPOSURE (EX4) ANALYSIS FOR METHIDATHION
Residue file name: METHWATA Analysis date: 06-14-2000
1989-92 DATA Adjustment factor #2 NOT used
DPR NOEL (Acute) = 0.300000 mg/kg body-wt/day

FEMALES (13-19 YRS/NP/NN)

	Daily Exposure Analysis (mg/kg body-weight/day) per Capita	per User
Mean	0.000015	0.000015
Standard Deviation	0.000008	0.000008
Standard Error	0.000000	0.000000

Percent of Person-Days that are User-Days =100.00%

ESTIMATED PERCENTILE OF USER-DAYS LESS THAN/EQUAL TO CALCULATED EXPOSURE
in mg/kg body-wt/day and corresponding Margin of Exposure (MOE)

PERCENTILE	EXPOSURE	MOE 2/	PERCENTILE	EXPOSURE	MOE
10.00	0.000006	50,453	90.00	0.000025	12,046
20.00	0.000008	36,747	95.00	0.000029	10,402
30.00	0.000010	30,989	97.50	0.000033	9,031
40.00	0.000011	26,745	99.00	0.000043	7,013
50.00	0.000013	22,809	99.50	0.000054	5,557
60.00	0.000015	19,480	99.75	0.000057	5,278
70.00	0.000018	16,629	99.90	0.000059	5,124
80.00	0.000021	14,270			

ESTIMATED PERCENTILE OF PER-CAPITA DAYS LESS THAN/EQUAL TO CALCULATED EXPOSURE
in mg/kg body-wt/day and corresponding Margin of Exposure (MOE)

PERCENTILE	EXPOSURE	MOE 2/	PERCENTILE	EXPOSURE	MOE
10.00	0.000006	50,453	90.00	0.000025	12,046
20.00	0.000008	36,747	95.00	0.000029	10,402
30.00	0.000010	30,989	97.50	0.000033	9,031
40.00	0.000011	26,745	99.00	0.000043	7,013
50.00	0.000013	22,809	99.50	0.000054	5,557
60.00	0.000015	19,480	99.75	0.000057	5,278
70.00	0.000018	16,629	99.90	0.000059	5,124
80.00	0.000021	14,270			

ACUTE EXPOSURE (EX4) ANALYSIS FOR METHIDATHION
Residue file name: METHWATA Analysis date: 06-14-2000
1989-92 DATA Adjustment factor #2 NOT used
DPR NOEL (Acute) = 0.300000 mg/kg body-wt/day

MALES (20+ YEARS)

	Daily Exposure Analysis (mg/kg body-weight/day) per Capita	per User
Mean	0.000016	0.000016
Standard Deviation	0.000009	0.000009
Standard Error	0.000000	0.000000

Percent of Person-Days that are User-Days = 99.98%

ESTIMATED PERCENTILE OF USER-DAYS LESS THAN/EQUAL TO CALCULATED EXPOSURE
in mg/kg body-wt/day and corresponding Margin of Exposure (MOE)

PERCENTILE	EXPOSURE	MOE 2/	PERCENTILE	EXPOSURE	MOE
10.00	0.000007	40,369	90.00	0.000027	10,978
20.00	0.000009	31,972	95.00	0.000033	9,132
30.00	0.000011	27,093	97.50	0.000039	7,718
40.00	0.000013	23,242	99.00	0.000047	6,338
50.00	0.000015	20,436	99.50	0.000056	5,361
60.00	0.000017	18,165	99.75	0.000065	4,616
70.00	0.000019	15,973	99.90	0.000088	3,420
80.00	0.000022	13,617			

ESTIMATED PERCENTILE OF PER-CAPITA DAYS LESS THAN/EQUAL TO CALCULATED EXPOSURE
in mg/kg body-wt/day and corresponding Margin of Exposure (MOE)

PERCENTILE	EXPOSURE	MOE 2/	PERCENTILE	EXPOSURE	MOE
10.00	0.000007	40,446	90.00	0.000027	10,978
20.00	0.000009	31,983	95.00	0.000033	9,132
30.00	0.000011	27,099	97.50	0.000039	7,718
40.00	0.000013	23,246	99.00	0.000047	6,338
50.00	0.000015	20,439	99.50	0.000056	5,362
60.00	0.000017	18,167	99.75	0.000065	4,617
70.00	0.000019	15,974	99.90	0.000088	3,420
80.00	0.000022	13,618			

ACUTE EXPOSURE (EX4) ANALYSIS FOR METHIDATHION
Residue file name: METHWATA Analysis date: 06-14-2000
1989-92 DATA Adjustment factor #2 NOT used
DPR NOEL (Acute) = 0.300000 mg/kg body-wt/day

FEMALES (20+ YEARS/NP/NN)

	Daily Exposure Analysis (mg/kg body-weight/day) per Capita	per User
Mean	0.000018	0.000018
Standard Deviation	0.000010	0.000010
Standard Error	0.000000	0.000000

Percent of Person-Days that are User-Days = 99.99%

ESTIMATED PERCENTILE OF USER-DAYS LESS THAN/EQUAL TO CALCULATED EXPOSURE
in mg/kg body-wt/day and corresponding Margin of Exposure (MOE)

PERCENTILE	EXPOSURE	MOE 2/	PERCENTILE	EXPOSURE	MOE
10.00	0.000008	38,357	90.00	0.000029	10,281
20.00	0.000010	29,276	95.00	0.000034	8,741
30.00	0.000012	24,648	97.50	0.000040	7,543
40.00	0.000014	21,427	99.00	0.000050	6,007
50.00	0.000016	18,776	99.50	0.000060	5,019
60.00	0.000018	16,563	99.75	0.000076	3,961
70.00	0.000021	14,543	99.90	0.000091	3,297
80.00	0.000024	12,469			

ESTIMATED PERCENTILE OF PER-CAPITA DAYS LESS THAN/EQUAL TO CALCULATED EXPOSURE
in mg/kg body-wt/day and corresponding Margin of Exposure (MOE)

PERCENTILE	EXPOSURE	MOE 2/	PERCENTILE	EXPOSURE	MOE
10.00	0.000008	38,393	90.00	0.000029	10,281
20.00	0.000010	29,282	95.00	0.000034	8,741
30.00	0.000012	24,651	97.50	0.000040	7,543
40.00	0.000014	21,429	99.00	0.000050	6,007
50.00	0.000016	18,777	99.50	0.000060	5,019
60.00	0.000018	16,564	99.75	0.000076	3,961
70.00	0.000021	14,544	99.90	0.000091	3,297
80.00	0.000024	12,470			

ACUTE EXPOSURE (EX4) ANALYSIS FOR METHIDATHION
Residue file name: METHWATA Analysis date: 06-14-2000
1989-92 DATA Adjustment factor #2 NOT used
DPR NOEL (Acute) = 0.300000 mg/kg body-wt/day

SENIORS (55+)

	Daily Exposure Analysis (mg/kg body-weight/day) per Capita	per User
Mean	0.000017	0.000017
Standard Deviation	0.000008	0.000008
Standard Error	0.000000	0.000000

Percent of Person-Days that are User-Days = 99.99%

ESTIMATED PERCENTILE OF USER-DAYS LESS THAN/EQUAL TO CALCULATED EXPOSURE
in mg/kg body-wt/day and corresponding Margin of Exposure (MOE)

PERCENTILE	EXPOSURE	MOE 2/	PERCENTILE	EXPOSURE	MOE
10.00	0.000008	35,758	90.00	0.000027	11,313
20.00	0.000011	28,414	95.00	0.000031	9,719
30.00	0.000012	24,449	97.50	0.000035	8,453
40.00	0.000014	21,714	99.00	0.000042	7,112
50.00	0.000015	19,372	99.50	0.000054	5,562
60.00	0.000017	17,364	99.75	0.000071	4,255
70.00	0.000019	15,534	99.90	0.000095	3,145
80.00	0.000022	13,686			

ESTIMATED PERCENTILE OF PER-CAPITA DAYS LESS THAN/EQUAL TO CALCULATED EXPOSURE
in mg/kg body-wt/day and corresponding Margin of Exposure (MOE)

PERCENTILE	EXPOSURE	MOE 2/	PERCENTILE	EXPOSURE	MOE
10.00	0.000008	35,785	90.00	0.000027	11,314
20.00	0.000011	28,418	95.00	0.000031	9,719
30.00	0.000012	24,451	97.50	0.000035	8,453
40.00	0.000014	21,715	99.00	0.000042	7,113
50.00	0.000015	19,373	99.50	0.000054	5,562
60.00	0.000017	17,364	99.75	0.000071	4,255
70.00	0.000019	15,534	99.90	0.000095	3,145
80.00	0.000022	13,686			

```
ACUTE EXPOSURE (EX4) ANALYSIS FOR METHIDATHION
Residue file name: METHWATA                            Analysis date: 06-14-2000
1989-92 DATA   Adjustment factor #2 NOT used
DPR NOEL (Acute) =   0.300000 mg/kg body-wt/day
===============================================================================

CUSTOM DEMOGRAPHICS 1: Workers, 16+ yrs
All Seasons
All Regions
Sex: M/F-all/
All Races
Age-Low: 16 yrs   High: 110 yrs
---------------------------------------

                                   Daily Exposure Analysis
                                   (mg/kg body-weight/day)
                                   per Capita     per User
                                   ----------    ---------
            Mean                      0.000017     0.000017
            Standard Deviation        0.000010     0.000010
            Standard Error            0.000000     0.000000

    Percent of Person-Days that are User-Days = 99.99%


  ESTIMATED PERCENTILE OF USER-DAYS LESS THAN/EQUAL TO CALCULATED EXPOSURE
     in mg/kg body-wt/day and corresponding Margin of Exposure (MOE)

 PERCENTILE    EXPOSURE    MOE 2/        PERCENTILE    EXPOSURE    MOE
 ----------  ----------  ---------       ----------  ----------  ---------
    10.00      0.000007     40,476          90.00      0.000028     10,641
    20.00      0.000010     31,126          95.00      0.000034      8,903
    30.00      0.000012     26,061          97.50      0.000040      7,502
    40.00      0.000013     22,452          99.00      0.000049      6,155
    50.00      0.000015     19,728          99.50      0.000059      5,087
    60.00      0.000017     17,403          99.75      0.000074      4,069
    70.00      0.000020     15,234          99.90      0.000087      3,462
    80.00      0.000023     13,043
```

ESTIMATED PERCENTILE OF PER-CAPITA DAYS LESS THAN/EQUAL TO CALCULATED EXPOSURE
in mg/kg body-wt/day and corresponding Margin of Exposure (MOE)

PERCENTILE	EXPOSURE	MOE 2/	PERCENTILE	EXPOSURE	MOE
10.00	0.000007	40,528	90.00	0.000028	10,641
20.00	0.000010	31,135	95.00	0.000034	8,903
30.00	0.000012	26,065	97.50	0.000040	7,502
40.00	0.000013	22,454	99.00	0.000049	6,155
50.00	0.000015	19,730	99.50	0.000059	5,087
60.00	0.000017	17,404	99.75	0.000074	4,069
70.00	0.000020	15,234	99.90	0.000087	3,462
80.00	0.000023	13,043			

Chronic Exposure (EX1) Analysis for Methidathion
RESIDUE FILE NAME: METHWATC ANALYSIS DATE: 06-14-2000
NFCS Combined 89-92 DATA
EPA Reference dose (RfD, chronic) = 0.001500 mg/kg body-wt/day
DPR NOEL (Chronic) = 0.150000 mg/kg body-wt/day
COMMENT 1: Surface Drinking Water

RESIDUE FILE LISTING

TAS CODE	CROP GRP	FOOD NAME	RESIDUE (PPM)	ADJ. FCTRS #1	#2	SOURCE CODE
432	A	WATER-BOTTLED	0.000029	1.00	1.00	
433	A	WATER-TAP	0.000029	1.00	1.00	
434	A	WATER-COMMERCIAL PROCESSING	0.000029	1.00	1.00	
435	A	WATER-NON-FOOD BASED	0.000029	1.00	1.00	

Chronic Exposure (EX1) Analysis for Methidathion
RESIDUE FILE NAME: METHWATC ANALYSIS DATE: 06-14-2000
NFCS Combined 89-92 DATA
EPA Reference dose (RfD, chronic) = 0.001500 mg/kg body-wt/day
DPR NOEL (Chronic) = 0.150000 mg/kg body-wt/day
COMMENT 1: Surface Drinking Water

TOTAL EXPOSURE BY POPULATION SUBGROUP

POPULATION SUBGROUP	TOTAL EXPOSURE mg/kg body-wt/day	Margin of Exposure 1/	Percent of RfD
U.S. POP - 48 STATES - ALL SEASONS	0.000001	177,814	0.1%
U.S. POPULATION - SPRING SEASON	0.000001	171,787	0.1%
U.S. POPULATION - SUMMER SEASON	0.000001	172,875	0.1%
U.S. POPULATION - AUTUMN SEASON	0.000001	180,438	0.1%
U.S. POPULATION - WINTER SEASON	0.000001	186,509	0.1%
NORTHEAST REGION	0.000001	191,693	0.1%
MIDWEST REGION	0.000001	177,601	0.1%
SOUTHERN REGION	0.000001	173,268	0.1%
WESTERN REGION	0.000001	179,185	0.1%
PACIFIC REGION	0.000001	180,095	0.1%
HISPANICS	0.000001	157,463	0.1%
NON-HISPANIC WHITES	0.000001	182,490	0.1%
NON-HISPANIC BLACKS	0.000001	167,881	0.1%
NON-HISPANIC OTHER THAN BLACK OR WHITE	0.000001	167,633	0.1%
ALL INFANTS	0.000003	48,758	0.2%
NURSING INFANTS (<1 YEAR OLD)	0.000001	175,599	0.1%
NON-NURSING INFANTS (<1 YEAR OLD)	0.000004	38,460	0.3%
CHILDREN (1-6 YEARS)	0.000001	117,097	0.1%
CHILDREN (7-12 YEARS)	0.000001	172,140	0.1%
FEMALES (13-19 YRS/NOT PREG. OR NURSING)	0.000001	226,766	0.0%
FEMALES (20+ YEARS/NOT PREG. OR NURSING)	0.000001	192,206	0.1%
FEMALES (13-50 YEARS)	0.000001	195,919	0.1%
FEMALES (13+/PREGNANT/NOT NURSING)	0.000001	214,527	0.0%
FEMALES (13+/NURSING)	0.000001	175,670	0.1%
MALES (13-19 YEARS)	0.000001	219,384	0.0%
MALES (20+ YEARS)	0.000001	205,701	0.0%
SENIORS (55+)	0.000001	201,132	0.0%

1. Margin of Exposure = DPR NOEL / Dietary Exposure

```
Chronic Exposure (EX1) Analysis for Methidathion
RESIDUE FILE NAME: METHWATC                          ANALYSIS DATE: 06-21-2000
NFCS Combined 89-92 DATA
Q1 = 0.340000
COMMENT 1: Surface Drinking Water
```

TOTAL EXPOSURE BY POPULATION SUBGROUP

POPULATION SUBGROUP	TOTAL EXPOSURE mg/kg body-wt/day	TOTAL EXPOSURE Life-Time Risk (Q_1=0.340000)
U.S. POP - 48 STATES - ALL SEASONS	0.000001	2.87E-07
U.S. POPULATION - SPRING SEASON	0.000001	2.97E-07
U.S. POPULATION - SUMMER SEASON	0.000001	2.95E-07
U.S. POPULATION - AUTUMN SEASON	0.000001	2.83E-07
U.S. POPULATION - WINTER SEASON	0.000001	2.73E-07
NORTHEAST REGION	0.000001	2.66E-07
MIDWEST REGION	0.000001	2.87E-07
SOUTHERN REGION	0.000001	2.94E-07
WESTERN REGION	0.000001	2.85E-07
PACIFIC REGION	0.000001	2.83E-07
HISPANICS	0.000001	3.24E-07
NON-HISPANIC WHITES	0.000001	2.79E-07
NON-HISPANIC BLACKS	0.000001	3.04E-07
NON-HISPANIC OTHER THAN BLACK OR WHITE	0.000001	3.04E-07
ALL INFANTS	0.000003	1.05E-06
NURSING INFANTS (<1 YEAR OLD)	0.000001	2.90E-07
NON-NURSING INFANTS (<1 YEAR OLD)	0.000004	1.33E-06
CHILDREN (1-6 YEARS)	0.000001	4.36E-07
CHILDREN (7-12 YEARS)	0.000001	2.96E-07
FEMALES (13-19 YRS/NOT PREG. OR NURSING)	0.000001	2.25E-07
FEMALES (20+ YEARS/NOT PREG. OR NURSING)	0.000001	2.65E-07
FEMALES (13-50 YEARS)	0.000001	2.60E-07
FEMALES (13+/PREGNANT/NOT NURSING)	0.000001	2.38E-07
FEMALES (13+/NURSING)	0.000001	2.90E-07
MALES (13-19 YEARS)	0.000001	2.32E-07
MALES (20+ YEARS)	0.000001	2.48E-07
SENIORS (55+)	0.000001	2.54E-07

Chronic Exposure (EX1) Analysis for Methidathion
RESIDUE FILE NAME: METHWATC ANALYSIS DATE: 06-21-2000
NFCS Combined 89-92 DATA
Q_1^* = 0.530000
COMMENT 1: Surface Drinking Water

TOTAL EXPOSURE BY POPULATION SUBGROUP

POPULATION SUBGROUP	TOTAL EXPOSURE mg/kg body-wt/day	TOTAL EXPOSURE Life-Time Risk (Q_1^*=0.530000)
U.S. POP - 48 STATES - ALL SEASONS	0.000001	4.47E-07
U.S. POPULATION - SPRING SEASON	0.000001	4.63E-07
U.S. POPULATION - SUMMER SEASON	0.000001	4.60E-07
U.S. POPULATION - AUTUMN SEASON	0.000001	4.41E-07
U.S. POPULATION - WINTER SEASON	0.000001	4.26E-07
NORTHEAST REGION	0.000001	4.15E-07
MIDWEST REGION	0.000001	4.48E-07
SOUTHERN REGION	0.000001	4.59E-07
WESTERN REGION	0.000001	4.44E-07
PACIFIC REGION	0.000001	4.41E-07
HISPANICS	0.000001	5.05E-07
NON-HISPANIC WHITES	0.000001	4.36E-07
NON-HISPANIC BLACKS	0.000001	4.74E-07
NON-HISPANIC OTHER THAN BLACK OR WHITE	0.000001	4.74E-07
ALL INFANTS	0.000003	1.63E-06
NURSING INFANTS (<1 YEAR OLD)	0.000001	4.53E-07
NON-NURSING INFANTS (<1 YEAR OLD)	0.000004	2.07E-06
CHILDREN (1-6 YEARS)	0.000001	6.79E-07
CHILDREN (7-12 YEARS)	0.000001	4.62E-07
FEMALES (13-19 YRS/NOT PREG. OR NURSING)	0.000001	3.51E-07
FEMALES (20+ YEARS/NOT PREG. OR NURSING)	0.000001	4.14E-07
FEMALES (13-50 YEARS)	0.000001	4.06E-07
FEMALES (13+/PREGNANT/NOT NURSING)	0.000001	3.71E-07
FEMALES (13+/NURSING)	0.000001	4.53E-07
MALES (13-19 YEARS)	0.000001	3.62E-07
MALES (20+ YEARS)	0.000001	3.86E-07
SENIORS (55+)	0.000001	3.95E-07

```
ACUTE EXPOSURE (EX4) ANALYSIS FOR METHIDATHION
Residue file name: METHATAG                           Analysis date: 06-15-2000
1989-92 DATA   Adjustment factor #2 NOT used
DPR NOEL (Acute) =   0.300000 mg/kg body-wt/day
COMMENT 1: Aggregate Dietary (Tier 1) and Drinking
===============================================================================
                         RESIDUE FILE LISTING
-------------------------------------------------------------------------------
```

TAS CODE	CROP GRP	FOOD NAME	RESIDUE (PPM)	ADJ. FCTRS #1	#2	SOURCE CODE
20	K	CITRUS CITRON	no consumption in survey			
22	K	GRAPEFRUIT-PEELED FRUIT	0.128000	0.10	1.00	DPR95%
23	K	GRAPEFRUIT-JUICE	0.128000	0.10	1.00	DPR95%
24	K	KUMQUATS	no consumption in survey			
26	K	LEMONS-PEELED FRUIT	0.057000	0.10	1.00	DPR95%
27	K	LEMONS-PEEL	0.057000	2.50	1.00	DPR95%
28	K	LEMONS-JUICE	0.057000	0.10	1.00	DPR95%
30	K	LIMES-PEELED FRUIT	0.026000	0.10	1.00	DPR95%
31	K	LIMES-PEEL	0.026000	2.50	1.00	DPR95%
32	K	LIMES-JUICE	0.026000	0.10	1.00	DPR95%
33	K	ORANGES-JUICE-CONCENTRATE	0.564000	0.37	1.00	DPR95%
34	K	ORANGES-PEELED FRUIT	0.564000	0.10	1.00	DPR95%
35	K	ORANGES-PEEL	0.564000	2.50	1.00	DPR95%
36	K	ORANGES-JUICE	0.564000	0.10	1.00	DPR95%
37	K	TANGELOS	no consumption in survey			
38	K	TANGERINES	1.030000	0.10	1.00	DPR
39	K	TANGERINES-JUICE	1.030000	0.10	1.00	DPR
40	R	ALMONDS	0.050000	1.00	1.00	TOLERA
41	R	BRAZIL NUTS	0.050000	1.00	1.00	TOLERA
42	R	CASHEWS	0.050000	1.00	1.00	TOLERA
43	R	CHESTNUTS	0.050000	1.00	1.00	TOLERA
44	R	FILBERTS (HAZELNUTS)	0.050000	1.00	1.00	TOLERA
45	R	HICKORY NUTS	0.050000	1.00	1.00	TOLERA
46	R	MACADAMIA NUTS (BUSH NUTS)	0.050000	1.00	1.00	TOLERA
47	R	PECANS	0.050000	1.00	1.00	TOLERA
48	R	WALNUTS	0.050000	1.00	1.00	TOLERA
49	R	BUTTER NUTS	no consumption in survey			
50	A	PISTACHIO NUTS	0.050000	1.00	1.00	TOLERA
51	R	BEECHNUTS	no consumption in survey			
52	L	APPLES	0.010000	1.00	1.00	DPR
53	L	APPLES-DRIED	0.010000	8.00	1.00	DPR
54	L	APPLES-JUICE/CIDER	0.010000	1.30	1.00	DPR
55	L	CRABAPPLES	no consumption in survey			
56	L	PEARS	0.012000	1.00	1.00	DPR95%
57	L	PEARS-DRIED	0.012000	6.25	1.00	DPR95%
58	L	QUINCES	no consumption in survey			

TAS CODE	CROP GRP	FOOD NAME	RESIDUE (PPM)	ADJ. FCTRS #1	#2	SOURCE CODE
59	M	APRICOTS	0.010000	1.00	1.00	DPR
60	M	APRICOTS-DRIED	0.010000	6.00	1.00	DPR
61	M	CHERRIES	0.010000	1.00	1.00	DPR
62	M	CHERRIES-DRIED	no consumption in survey			
63	M	CHERRIES-JUICE	0.010000	1.50	1.00	DPR
64	M	NECTARINES	0.010000	1.00	1.00	DPR
65	M	PEACHES	0.010000	1.00	1.00	DPR
66	M	PEACHES-DRIED	0.010000	7.00	1.00	DPR
67	M	PLUMS(DAMSONS)	0.010000	1.00	1.00	DPR
68	M	PLUMS-PRUNES(DRIED)	0.010000	5.00	1.00	DPR
69	M	PLUMS/PRUNE-JUICE	0.010000	1.40	1.00	DPR
80	A	MANGOES	0.050000	1.00	1.00	TOLERA
82	A	OLIVES	0.050000	1.00	1.00	TOLERA
97	A	KIWI FRUIT	0.010000	1.00	1.00	DPR
103	A	SUGAR APPLES (SWEETSOP)	no consumption in survey			
106	A	CARAMBOLA (STARFRUIT)	no consumption in survey			
108	A	LONGAN FRUIT	no consumption in survey			
181	A	ARTICHOKES-GLOBE	0.040000	1.00	1.00	DPR
203	B	ARTICHOKES-JERUSALEM	no consumption in survey			
246	A	SUNFLOWER-SEEDS-WITH HULLS	no consumption in survey			
275	O	SORGHUM (INCLUDING MILO)	no consumption in survey			
290	A	COTTONSEED-OIL	0.200000	1.00	1.00	TOLERA
291	A	COTTONSEED-MEAL	0.200000	1.00	1.00	TOLERA
294	A	SAFFLOWER-SEED	no consumption in survey			
295	A	SAFFLOWER-OIL	0.500000	1.00	1.00	TOLERA
298	A	SUNFLOWER-OIL	0.500000	1.00	1.00	TOLERA
300	A	OLIVE OIL	0.050000	1.00	1.00	TOLERA
318	X	MILK-NONFAT SOLIDS	0.000350	7.87	1.00	REGIST
319	X	MILK-FAT SOLIDS	0.000350	7.87	1.00	REGIST
320	X	MILK SUGAR (LACTOSE)	0.000350	8.13	1.00	REGIST
321	U	BEEF-MEAT BYPRODUCTS	0.000920	1.00	1.00	REGIST
322	U	BEEF(ORGAN MEATS)-OTHER	0.000920	1.00	1.00	REGIST
323	U	BEEF-DRIED	0.000920	1.92	1.00	REGIST
324	U	BEEF(BONELESS)-FAT	0.000100	1.00	1.00	REGIST
325	U	BEEF(ORGAN MEATS)-KIDNEY	0.000600	1.00	1.00	REGIST
326	U	BEEF(ORGAN MEATS)-LIVER	0.000920	1.00	1.00	REGIST
327	U	BEEF(BONELESS)-LEAN (FAT/FREE)	0.000920	1.00	1.00	REGIST
328	U	GOAT-MEAT BYPRODUCTS	no consumption in survey			
329	U	GOAT(ORGAN MEATS)-OTHER	0.000920	1.00	1.00	REGIST
330	U	GOAT(BONELESS)-FAT	no consumption in survey			
331	U	GOAT(ORGAN MEATS)-KIDNEY	no consumption in survey			
332	U	GOAT(ORGAN MEATS)-LIVER	no consumption in survey			
333	U	GOAT(BONELESS)-LEAN (FAT/FREE)	no consumption in survey			
334	U	HORSE	no consumption in survey			
336	U	SHEEP-MEAT BYPRODUCTS	no consumption in survey			
337	U	SHEEP(ORGAN MEATS)-OTHER	no consumption in survey			

TAS CODE	CROP GRP	FOOD NAME	RESIDUE (PPM)	ADJ. FCTRS #1	ADJ. FCTRS #2	SOURCE CODE
338	U	SHEEP(BONELESS)-FAT	0.000100	1.00	1.00	REGIST
339	U	SHEEP(ORGAN MEATS)-KIDNEY	no consumption in survey			
340	U	SHEEP(ORGAN MEATS)-LIVER	no consumption in survey			
341	U	SHEEP(BONELESS)-LEAN (FAT FREE	0.000920	1.00	1.00	REGIST
342	U	PORK-MEAT BYPRODUCTS	0.000440	1.00	1.00	REGIST
343	U	PORK(ORGAN MEATS)-OTHER	no consumption in survey			
344	U	PORK(BONELESS)-FAT	0.000050	1.00	1.00	REGIST
345	U	PORK(ORGAN MEATS)-KIDNEY	no consumption in survey			
346	U	PORK(ORGAN MEATS)-LIVER	0.000440	1.00	1.00	REGIST
347	U	PORK(BONELESS)-LEAN (FAT FREE)	0.000440	1.00	1.00	REGIST
355	V	TURKEY-BYPRODUCTS	0.000210	1.00	1.00	REGIST
356	V	TURKEY-GIBLETS (LIVER)	0.000210	1.00	1.00	REGIST
357	V	TURKEY-(BONELESS)-FAT	0.000070	1.00	1.00	REGIST
358	V	TURKEY-(BONELESS)LEAN/FAT FREE	0.000110	1.00	1.00	REGIST
359	V	TURKEY-UNSPECIFIED	no consumption in survey			
360	V	POULTRY-OTHER-LEAN (FAT FREE)	0.000110	1.00	1.00	REGIST
361	V	POULTRY-OTHER-GIBLETS(LIVER)	no consumption in survey			
362	V	POULTRY-OTHER-FAT	0.000070	1.00	1.00	REGIST
363	X	EGGS-WHOLE	0.000130	1.00	1.00	REGIST
364	X	EGGS-WHITE ONLY	0.000130	1.00	1.00	REGIST
365	X	EGGS-YOLK ONLY	0.000130	1.00	1.00	REGIST
366	V	CHICKEN-BYPRODUCTS	no consumption in survey			
367	V	CHICKEN-GIBLETS(LIVER)	0.000210	1.00	1.00	REGIST
368	V	CHICKEN (BONELESS)-FAT	0.000070	1.00	1.00	REGIST
369	V	CHICKEN(BONELESS)LEAN/FAT FREE	0.000110	1.00	1.00	REGIST
377	L	APPLES-JUICE-CONCENTRATE	0.010000	3.90	1.00	DPR
385	V	CHICKEN-GIBLETS (EXCL. LIVER)	0.000210	1.00	1.00	REGIST
398	X	MILK-BASED WATER	0.000350	1.00	1.00	REGIST
402	M	PEACHES-JUICE	0.010000	1.00	1.00	DPR
404	L	PEARS-NECTAR	0.012000	1.00	1.00	DPR95%
410	M	APRICOT JUICE OR NECTAR	0.010000	1.00	1.00	DPR
417	A	SUNFLOWER-SEEDS-HULLED	0.500000	1.00	1.00	TOLERA
420	K	TANGERINES-JUICE-CONCENTRATE	no consumption in survey			
424	U	VEAL-(BONELESS)-FAT	0.000100	1.00	1.00	REGIST
425	U	VEAL-(BONELESS)-LEAN (FAT FREE	0.000920	1.00	1.00	REGIST
426	U	VEAL-(ORGAN MEATS)-KIDNEY	no consumption in survey			
427	U	VEAL-(ORGAN MEATS)-LIVER	no consumption in survey			
428	U	VEAL-(ORGAN MEATS)-OTHER	no consumption in survey			
429	U	VEAL-DRIED	no consumption in survey			
430	U	VEAL-MEAT BYPRODUCTS	no consumption in survey			
431	R	WALNUT OIL	no consumption in survey			
432	A	WATER-BOTTLED	no consumption in survey			
433	A	WATER-TAP	0.000654	1.00	1.00	DPR

ACUTE EXPOSURE (EX4) ANALYSIS FOR METHIDATHION
Residue file name: METHATAG Analysis date: 06-15-2000
1989-92 DATA Adjustment factor #2 NOT used
DPR NOEL (Acute) = 0.300000 mg/kg body-wt/day
Initial estimate of user-days as % of person-days in survey = 100.00%
COMMENT 1: Aggregate Dietary (Tier 1) and Drinking

U.S. POP - ALL SEASONS

	Daily Exposure Analysis 1/ (mg/kg body-weight/day) per Capita	per User
Mean	0.000121	0.000121
Standard Deviation	0.000192	0.000192
Standard Error	0.000001	0.000001

Percent of Person-Days that are User-Days = 99.85%

ESTIMATED PERCENTILE OF USER-DAYS LESS THAN/EQUAL TO CALCULATED EXPOSURE
in mg/kg body-wt/day and corresponding Margin of Exposure (MOE)

PERCENTILE	EXPOSURE	MOE 2/	PERCENTILE	EXPOSURE	MOE
10.00	0.000017	17,591	90.00	0.000293	1,024
20.00	0.000023	12,802	95.00	0.000441	681
30.00	0.000030	9,933	97.50	0.000627	478
40.00	0.000039	7,752	99.00	0.000933	322
50.00	0.000051	5,872	99.50	0.001207	249
60.00	0.000071	4,219	99.75	0.001449	207
70.00	0.000114	2,633	99.90	0.001886	159
80.00	0.000182	1,650			

ESTIMATED PERCENTILE OF PER-CAPITA DAYS LESS THAN/EQUAL TO CALCULATED EXPOSURE
in mg/kg body-wt/day and corresponding Margin of Exposure (MOE)

PERCENTILE	EXPOSURE	MOE 2/	PERCENTILE	EXPOSURE	MOE
10.00	0.000017	17,832	90.00	0.000293	1,025
20.00	0.000023	12,844	95.00	0.000441	681
30.00	0.000030	9,956	97.50	0.000627	479
40.00	0.000039	7,767	99.00	0.000932	322
50.00	0.000051	5,883	99.50	0.001207	249
60.00	0.000071	4,227	99.75	0.001449	207
70.00	0.000114	2,637	99.90	0.001886	159
80.00	0.000182	1,652			

1/ Analysis based on all participant-days in NFCS 1989-92 survey.
2/ Margin of Exposure = NOEL/ Dietary Exposure.

ACUTE EXPOSURE (EX4) ANALYSIS FOR METHIDATHION
Residue file name: METHATAG Analysis date: 06-15-2000
1989-92 DATA Adjustment factor #2 NOT used
DPR NOEL (Acute) = 0.300000 mg/kg body-wt/day

WESTERN REGION

	Daily Exposure Analysis (mg/kg body-weight/day) per Capita	per User
Mean	0.000132	0.000132
Standard Deviation	0.000209	0.000209
Standard Error	0.000002	0.000002

Percent of Person-Days that are User-Days = 99.71%

ESTIMATED PERCENTILE OF USER-DAYS LESS THAN/EQUAL TO CALCULATED EXPOSURE
in mg/kg body-wt/day and corresponding Margin of Exposure (MOE)

PERCENTILE	EXPOSURE	MOE 2/	PERCENTILE	EXPOSURE	MOE
10.00	0.000017	17,835	90.00	0.000311	964
20.00	0.000024	12,622	95.00	0.000483	622
30.00	0.000031	9,620	97.50	0.000726	413
40.00	0.000041	7,362	99.00	0.001066	281
50.00	0.000054	5,579	99.50	0.001391	216
60.00	0.000078	3,864	99.75	0.001722	174
70.00	0.000126	2,378	99.90	0.002086	144
80.00	0.000194	1,543			

ESTIMATED PERCENTILE OF PER-CAPITA DAYS LESS THAN/EQUAL TO CALCULATED EXPOSURE
in mg/kg body-wt/day and corresponding Margin of Exposure (MOE)

PERCENTILE	EXPOSURE	MOE 2/	PERCENTILE	EXPOSURE	MOE
10.00	0.000016	18,308	90.00	0.000311	965
20.00	0.000024	12,707	95.00	0.000482	622
30.00	0.000031	9,666	97.50	0.000725	414
40.00	0.000041	7,391	99.00	0.001066	282
50.00	0.000054	5,598	99.50	0.001390	216
60.00	0.000077	3,878	99.75	0.001721	174
70.00	0.000126	2,386	99.90	0.002085	144
80.00	0.000194	1,546			

ACUTE EXPOSURE (EX4) ANALYSIS FOR METHIDATHION
Residue file name: METHATAG Analysis date: 06-15-2000
1989-92 DATA Adjustment factor #2 NOT used
DPR NOEL (Acute) = 0.300000 mg/kg body-wt/day

NURSING INFANTS (<1 YEAR)

	Daily Exposure Analysis (mg/kg body-weight/day) per Capita	per User
Mean	0.000143	0.000225
Standard Deviation	0.000747	0.000927
Standard Error	0.000063	0.000095

Percent of Person-Days that are User-Days = 63.57%

ESTIMATED PERCENTILE OF USER-DAYS LESS THAN/EQUAL TO CALCULATED EXPOSURE
in mg/kg body-wt/day and corresponding Margin of Exposure (MOE)

PERCENTILE	EXPOSURE	MOE 2/	PERCENTILE	EXPOSURE	MOE
10.00	0.000008	38,057	90.00	0.000352	853
20.00	0.000011	28,527	95.00	0.000878	342
30.00	0.000013	22,813	97.50	0.001345	223
40.00	0.000017	17,706	99.00	0.002387	126
50.00	0.000029	10,227	99.50	0.005476	55
60.00	0.000039	7,710	99.75	0.007769	39
70.00	0.000086	3,494	99.90	0.009144	33
80.00	0.000204	1,469			

ESTIMATED PERCENTILE OF PER-CAPITA DAYS LESS THAN/EQUAL TO CALCULATED EXPOSURE
in mg/kg body-wt/day and corresponding Margin of Exposure (MOE)

PERCENTILE	EXPOSURE	MOE 2/	PERCENTILE	EXPOSURE	MOE
10.00	0.000000	>1,000,000	90.00	0.000267	1,123
20.00	0.000000	>1,000,000	95.00	0.000577	520
30.00	0.000000	>1,000,000	97.50	0.001078	278
40.00	0.000004	67,827	99.00	0.001989	151
50.00	0.000011	27,599	99.50	0.003705	81
60.00	0.000016	18,947	99.75	0.006455	46
70.00	0.000032	9,369	99.90	0.008618	35
80.00	0.000079	3,798			

ACUTE EXPOSURE (EX4) ANALYSIS FOR METHIDATHION
Residue file name: METHATAG Analysis date: 06-15-2000
1989-92 DATA Adjustment factor #2 NOT used
DPR NOEL (Acute) = 0.300000 mg/kg body-wt/day

NON-NURSING INFANTS (<1)

Daily Exposure Analysis (mg/kg body-weight/day)

	per Capita	per User
Mean	0.000298	0.000298
Standard Deviation	0.000280	0.000280
Standard Error	0.000013	0.000013

Percent of Person-Days that are User-Days =100.00%

ESTIMATED PERCENTILE OF USER-DAYS LESS THAN/EQUAL TO CALCULATED EXPOSURE
in mg/kg body-wt/day and corresponding Margin of Exposure (MOE)

PERCENTILE	EXPOSURE	MOE 2/	PERCENTILE	EXPOSURE	MOE
10.00	0.000100	2,998	90.00	0.000576	521
20.00	0.000130	2,308	95.00	0.000916	328
30.00	0.000145	2,071	97.50	0.001225	245
40.00	0.000158	1,902	99.00	0.001351	222
50.00	0.000191	1,574	99.50	0.001813	165
60.00	0.000257	1,167	99.75	0.001864	161
70.00	0.000320	937	99.90	0.001895	158
80.00	0.000403	744			

ESTIMATED PERCENTILE OF PER-CAPITA DAYS LESS THAN/EQUAL TO CALCULATED EXPOSURE
in mg/kg body-wt/day and corresponding Margin of Exposure (MOE)

PERCENTILE	EXPOSURE	MOE 2/	PERCENTILE	EXPOSURE	MOE
10.00	0.000100	2,998	90.00	0.000576	521
20.00	0.000130	2,308	95.00	0.000916	328
30.00	0.000145	2,071	97.50	0.001225	245
40.00	0.000158	1,902	99.00	0.001351	222
50.00	0.000191	1,574	99.50	0.001813	165
60.00	0.000257	1,167	99.75	0.001864	161
70.00	0.000320	937	99.90	0.001895	158
80.00	0.000403	744			

ACUTE EXPOSURE (EX4) ANALYSIS FOR METHIDATHION
Residue file name: METHATAG Analysis date: 06-15-2000
1989-92 DATA Adjustment factor #2 NOT used
DPR NOEL (Acute) = 0.300000 mg/kg body-wt/day

FEMALES (13+/PREG/NOT NSG)

	Daily Exposure Analysis (mg/kg body-weight/day) per Capita	per User
Mean	0.000110	0.000110
Standard Deviation	0.000129	0.000129
Standard Error	0.000007	0.000007

Percent of Person-Days that are User-Days =100.00%

ESTIMATED PERCENTILE OF USER-DAYS LESS THAN/EQUAL TO CALCULATED EXPOSURE
in mg/kg body-wt/day and corresponding Margin of Exposure (MOE)

PERCENTILE	EXPOSURE	MOE 2/	PERCENTILE	EXPOSURE	MOE
10.00	0.000017	17,210	90.00	0.000283	1,061
20.00	0.000022	13,695	95.00	0.000371	809
30.00	0.000031	9,604	97.50	0.000463	647
40.00	0.000042	7,103	99.00	0.000507	591
50.00	0.000050	6,033	99.50	0.000638	470
60.00	0.000063	4,766	99.75	0.000855	351
70.00	0.000123	2,445	99.90	0.000944	318
80.00	0.000192	1,565			

ESTIMATED PERCENTILE OF PER-CAPITA DAYS LESS THAN/EQUAL TO CALCULATED EXPOSURE
in mg/kg body-wt/day and corresponding Margin of Exposure (MOE)

PERCENTILE	EXPOSURE	MOE 2/	PERCENTILE	EXPOSURE	MOE
10.00	0.000017	17,210	90.00	0.000283	1,061
20.00	0.000022	13,695	95.00	0.000371	809
30.00	0.000031	9,604	97.50	0.000463	647
40.00	0.000042	7,103	99.00	0.000507	591
50.00	0.000050	6,033	99.50	0.000638	470
60.00	0.000063	4,766	99.75	0.000855	351
70.00	0.000123	2,445	99.90	0.000944	318
80.00	0.000192	1,565			

ACUTE EXPOSURE (EX4) ANALYSIS FOR METHIDATHION
Residue file name: METHATAG Analysis date: 06-15-2000
1989-92 DATA Adjustment factor #2 NOT used
DPR NOEL (Acute) = 0.300000 mg/kg body-wt/day

FEMALES (13+/NURSING)

Daily Exposure Analysis (mg/kg body-weight/day)

	per Capita	per User
Mean	0.000149	0.000149
Standard Deviation	0.000174	0.000174
Standard Error	0.000012	0.000012

Percent of Person-Days that are User-Days =100.00%

ESTIMATED PERCENTILE OF USER-DAYS LESS THAN/EQUAL TO CALCULATED EXPOSURE
in mg/kg body-wt/day and corresponding Margin of Exposure (MOE)

PERCENTILE	EXPOSURE	MOE 2/	PERCENTILE	EXPOSURE	MOE
10.00	0.000017	17,215	90.00	0.000433	693
20.00	0.000024	12,673	95.00	0.000531	565
30.00	0.000033	9,124	97.50	0.000577	520
40.00	0.000044	6,891	99.00	0.000724	415
50.00	0.000063	4,780	99.50	0.000768	391
60.00	0.000106	2,832	99.75	0.000866	347
70.00	0.000176	1,709	99.90	0.000944	318
80.00	0.000259	1,157			

ESTIMATED PERCENTILE OF PER-CAPITA DAYS LESS THAN/EQUAL TO CALCULATED EXPOSURE
in mg/kg body-wt/day and corresponding Margin of Exposure (MOE)

PERCENTILE	EXPOSURE	MOE 2/	PERCENTILE	EXPOSURE	MOE
10.00	0.000017	17,215	90.00	0.000433	693
20.00	0.000024	12,673	95.00	0.000531	565
30.00	0.000033	9,124	97.50	0.000577	520
40.00	0.000044	6,891	99.00	0.000724	415
50.00	0.000063	4,780	99.50	0.000768	391
60.00	0.000106	2,832	99.75	0.000866	347
70.00	0.000176	1,709	99.90	0.000944	318
80.00	0.000259	1,157			

ACUTE EXPOSURE (EX4) ANALYSIS FOR METHIDATHION
Residue file name: METHATAG Analysis date: 06-15-2000
1989-92 DATA Adjustment factor #2 NOT used
DPR NOEL (Acute) = 0.300000 mg/kg body-wt/day

CHILDREN (1-6 YEARS)

	Daily Exposure Analysis (mg/kg body-weight/day) per Capita	per User
Mean	0.000319	0.000319
Standard Deviation	0.000378	0.000378
Standard Error	0.000006	0.000006

Percent of Person-Days that are User-Days =100.00%

ESTIMATED PERCENTILE OF USER-DAYS LESS THAN/EQUAL TO CALCULATED EXPOSURE
in mg/kg body-wt/day and corresponding Margin of Exposure (MOE)

PERCENTILE	EXPOSURE	MOE 2/	PERCENTILE	EXPOSURE	MOE
10.00	0.000047	6,345	90.00	0.000803	373
20.00	0.000065	4,641	95.00	0.001067	281
30.00	0.000082	3,676	97.50	0.001364	220
40.00	0.000107	2,803	99.00	0.001681	179
50.00	0.000151	1,983	99.50	0.002178	138
60.00	0.000228	1,315	99.75	0.002515	119
70.00	0.000364	824	99.90	0.002801	107
80.00	0.000548	548			

ESTIMATED PERCENTILE OF PER-CAPITA DAYS LESS THAN/EQUAL TO CALCULATED EXPOSURE
in mg/kg body-wt/day and corresponding Margin of Exposure (MOE)

PERCENTILE	EXPOSURE	MOE 2/	PERCENTILE	EXPOSURE	MOE
10.00	0.000047	6,345	90.00	0.000803	373
20.00	0.000065	4,641	95.00	0.001067	281
30.00	0.000082	3,676	97.50	0.001364	220
40.00	0.000107	2,803	99.00	0.001681	179
50.00	0.000151	1,983	99.50	0.002178	138
60.00	0.000228	1,315	99.75	0.002515	119
70.00	0.000364	824	99.90	0.002801	107
80.00	0.000548	548			

ACUTE EXPOSURE (EX4) ANALYSIS FOR METHIDATHION
Residue file name: METHATAG Analysis date: 06-15-2000
1989-92 DATA Adjustment factor #2 NOT used
DPR NOEL (Acute) = 0.300000 mg/kg body-wt/day

CHILDREN (7-12 YEARS)

	Daily Exposure Analysis (mg/kg body-weight/day) per Capita	per User
Mean	0.000184	0.000184
Standard Deviation	0.000232	0.000232
Standard Error	0.000004	0.000004

Percent of Person-Days that are User-Days =100.00%

ESTIMATED PERCENTILE OF USER-DAYS LESS THAN/EQUAL TO CALCULATED EXPOSURE
in mg/kg body-wt/day and corresponding Margin of Exposure (MOE)

PERCENTILE	EXPOSURE	MOE 2/	PERCENTILE	EXPOSURE	MOE
10.00	0.000028	10,553	90.00	0.000464	647
20.00	0.000039	7,715	95.00	0.000579	519
30.00	0.000051	5,878	97.50	0.000810	370
40.00	0.000068	4,386	99.00	0.001152	260
50.00	0.000089	3,366	99.50	0.001375	218
60.00	0.000125	2,399	99.75	0.001668	180
70.00	0.000184	1,633	99.90	0.001939	155
80.00	0.000310	968			

ESTIMATED PERCENTILE OF PER-CAPITA DAYS LESS THAN/EQUAL TO CALCULATED EXPOSURE
in mg/kg body-wt/day and corresponding Margin of Exposure (MOE)

PERCENTILE	EXPOSURE	MOE 2/	PERCENTILE	EXPOSURE	MOE
10.00	0.000028	10,553	90.00	0.000464	647
20.00	0.000039	7,715	95.00	0.000579	519
30.00	0.000051	5,878	97.50	0.000810	370
40.00	0.000068	4,386	99.00	0.001152	260
50.00	0.000089	3,366	99.50	0.001375	218
60.00	0.000125	2,399	99.75	0.001668	180
70.00	0.000184	1,633	99.90	0.001939	155
80.00	0.000310	968			

ACUTE EXPOSURE (EX4) ANALYSIS FOR METHIDATHION
Residue file name: METHATAG Analysis date: 06-15-2000
1989-92 DATA Adjustment factor #2 NOT used
DPR NOEL (Acute) = 0.300000 mg/kg body-wt/day

MALES (13-19 YEARS)

	Daily Exposure Analysis (mg/kg body-weight/day) per Capita	per User
Mean	0.000114	0.000114
Standard Deviation	0.000148	0.000148
Standard Error	0.000004	0.000004

Percent of Person-Days that are User-Days =100.00%

ESTIMATED PERCENTILE OF USER-DAYS LESS THAN/EQUAL TO CALCULATED EXPOSURE
in mg/kg body-wt/day and corresponding Margin of Exposure (MOE)

PERCENTILE	EXPOSURE	MOE 2/	PERCENTILE	EXPOSURE	MOE
10.00	0.000017	17,234	90.00	0.000284	1,055
20.00	0.000025	12,182	95.00	0.000391	768
30.00	0.000031	9,536	97.50	0.000491	611
40.00	0.000039	7,767	99.00	0.000621	483
50.00	0.000049	6,078	99.50	0.000774	388
60.00	0.000070	4,276	99.75	0.000960	312
70.00	0.000114	2,624	99.90	0.001032	291
80.00	0.000220	1,366			

ESTIMATED PERCENTILE OF PER-CAPITA DAYS LESS THAN/EQUAL TO CALCULATED EXPOSURE
in mg/kg body-wt/day and corresponding Margin of Exposure (MOE)

PERCENTILE	EXPOSURE	MOE 2/	PERCENTILE	EXPOSURE	MOE
10.00	0.000017	17,234	90.00	0.000284	1,055
20.00	0.000025	12,182	95.00	0.000391	768
30.00	0.000031	9,536	97.50	0.000491	611
40.00	0.000039	7,767	99.00	0.000621	483
50.00	0.000049	6,078	99.50	0.000774	388
60.00	0.000070	4,276	99.75	0.000960	312
70.00	0.000114	2,624	99.90	0.001032	291
80.00	0.000220	1,366			

ACUTE EXPOSURE (EX4) ANALYSIS FOR METHIDATHION
Residue file name: METHATAG Analysis date: 06-15-2000
1989-92 DATA Adjustment factor #2 NOT used
DPR NOEL (Acute) = 0.300000 mg/kg body-wt/day

FEMALES (13-19 YRS/NP/NN)

Daily Exposure Analysis (mg/kg body-weight/day)

	per Capita	per User
Mean	0.000101	0.000101
Standard Deviation	0.000135	0.000135
Standard Error	0.000003	0.000003

Percent of Person-Days that are User-Days =100.00%

ESTIMATED PERCENTILE OF USER-DAYS LESS THAN/EQUAL TO CALCULATED EXPOSURE
in mg/kg body-wt/day and corresponding Margin of Exposure (MOE)

PERCENTILE	EXPOSURE	MOE 2/	PERCENTILE	EXPOSURE	MOE
10.00	0.000015	19,777	90.00	0.000284	1,056
20.00	0.000020	14,735	95.00	0.000373	805
30.00	0.000025	11,814	97.50	0.000483	621
40.00	0.000031	9,618	99.00	0.000593	506
50.00	0.000039	7,643	99.50	0.000725	414
60.00	0.000052	5,766	99.75	0.000843	356
70.00	0.000089	3,390	99.90	0.001126	266
80.00	0.000177	1,691			

ESTIMATED PERCENTILE OF PER-CAPITA DAYS LESS THAN/EQUAL TO CALCULATED EXPOSURE
in mg/kg body-wt/day and corresponding Margin of Exposure (MOE)

PERCENTILE	EXPOSURE	MOE 2/	PERCENTILE	EXPOSURE	MOE
10.00	0.000015	19,777	90.00	0.000284	1,056
20.00	0.000020	14,735	95.00	0.000373	805
30.00	0.000025	11,814	97.50	0.000483	621
40.00	0.000031	9,618	99.00	0.000593	506
50.00	0.000039	7,643	99.50	0.000725	414
60.00	0.000052	5,766	99.75	0.000843	356
70.00	0.000089	3,390	99.90	0.001126	266
80.00	0.000177	1,691			

ACUTE EXPOSURE (EX4) ANALYSIS FOR METHIDATHION
Residue file name: METHATAG Analysis date: 06-15-2000
1989-92 DATA Adjustment factor #2 NOT used
DPR NOEL (Acute) = 0.300000 mg/kg body-wt/day

MALES (20+ YEARS)

	Daily Exposure Analysis (mg/kg body-weight/day) per Capita	per User
Mean	0.000081	0.000081
Standard Deviation	0.000100	0.000100
Standard Error	0.000001	0.000001

Percent of Person-Days that are User-Days = 99.99%

ESTIMATED PERCENTILE OF USER-DAYS LESS THAN/EQUAL TO CALCULATED EXPOSURE
in mg/kg body-wt/day and corresponding Margin of Exposure (MOE)

PERCENTILE	EXPOSURE	MOE 2/	PERCENTILE	EXPOSURE	MOE
10.00	0.000016	19,235	90.00	0.000207	1,452
20.00	0.000021	14,412	95.00	0.000273	1,099
30.00	0.000026	11,583	97.50	0.000350	856
40.00	0.000032	9,396	99.00	0.000448	669
50.00	0.000040	7,514	99.50	0.000547	548
60.00	0.000053	5,666	99.75	0.000698	430
70.00	0.000076	3,965	99.90	0.000853	352
80.00	0.000133	2,261			

ESTIMATED PERCENTILE OF PER-CAPITA DAYS LESS THAN/EQUAL TO CALCULATED EXPOSURE
in mg/kg body-wt/day and corresponding Margin of Exposure (MOE)

PERCENTILE	EXPOSURE	MOE 2/	PERCENTILE	EXPOSURE	MOE
10.00	0.000016	19,245	90.00	0.000207	1,452
20.00	0.000021	14,414	95.00	0.000273	1,099
30.00	0.000026	11,584	97.50	0.000350	856
40.00	0.000032	9,397	99.00	0.000448	669
50.00	0.000040	7,514	99.50	0.000547	548
60.00	0.000053	5,666	99.75	0.000698	430
70.00	0.000076	3,965	99.90	0.000853	352
80.00	0.000133	2,261			

ACUTE EXPOSURE (EX4) ANALYSIS FOR METHIDATHION
Residue file name: METHATAG Analysis date: 06-15-2000
1989-92 DATA Adjustment factor #2 NOT used
DPR NOEL (Acute) = 0.300000 mg/kg body-wt/day

FEMALES (20+ YEARS/NP/NN)

	Daily Exposure Analysis (mg/kg body-weight/day) per Capita	per User
Mean	0.000088	0.000088
Standard Deviation	0.000108	0.000108
Standard Error	0.000001	0.000001

Percent of Person-Days that are User-Days =100.00%

ESTIMATED PERCENTILE OF USER-DAYS LESS THAN/EQUAL TO CALCULATED EXPOSURE
in mg/kg body-wt/day and corresponding Margin of Exposure (MOE)

PERCENTILE	EXPOSURE	MOE 2/	PERCENTILE	EXPOSURE	MOE
10.00	0.000016	18,877	90.00	0.000233	1,290
20.00	0.000022	13,890	95.00	0.000296	1,013
30.00	0.000027	11,165	97.50	0.000369	814
40.00	0.000034	8,917	99.00	0.000499	601
50.00	0.000043	7,032	99.50	0.000610	492
60.00	0.000056	5,340	99.75	0.000754	398
70.00	0.000083	3,626	99.90	0.000893	336
80.00	0.000144	2,078			

ESTIMATED PERCENTILE OF PER-CAPITA DAYS LESS THAN/EQUAL TO CALCULATED EXPOSURE
in mg/kg body-wt/day and corresponding Margin of Exposure (MOE)

PERCENTILE	EXPOSURE	MOE 2/	PERCENTILE	EXPOSURE	MOE
10.00	0.000016	18,885	90.00	0.000233	1,290
20.00	0.000022	13,891	95.00	0.000296	1,013
30.00	0.000027	11,166	97.50	0.000369	814
40.00	0.000034	8,918	99.00	0.000499	601
50.00	0.000043	7,032	99.50	0.000610	492
60.00	0.000056	5,340	99.75	0.000754	398
70.00	0.000083	3,626	99.90	0.000893	336
80.00	0.000144	2,078			

```
ACUTE EXPOSURE (EX4) ANALYSIS FOR METHIDATHION
Residue file name: METHATAG                           Analysis date: 06-15-2000
1989-92 DATA   Adjustment factor #2 NOT used
DPR NOEL (Acute) =   0.300000 mg/kg body-wt/day
===============================================================================

SENIORS (55+)                     Daily Exposure Analysis
-------------                     (mg/kg body-weight/day)
                                  per Capita     per User
                                  ----------    ---------
            Mean                     0.000090     0.000090
            Standard Deviation       0.000093     0.000093
            Standard Error           0.000001     0.000001

    Percent of Person-Days that are User-Days = 99.99%
```

ESTIMATED PERCENTILE OF USER-DAYS LESS THAN/EQUAL TO CALCULATED EXPOSURE
in mg/kg body-wt/day and corresponding Margin of Exposure (MOE)

PERCENTILE	EXPOSURE	MOE 2/	PERCENTILE	EXPOSURE	MOE
10.00	0.000018	16,922	90.00	0.000225	1,336
20.00	0.000023	13,014	95.00	0.000280	1,073
30.00	0.000030	10,145	97.50	0.000332	902
40.00	0.000037	8,088	99.00	0.000402	747
50.00	0.000049	6,158	99.50	0.000459	654
60.00	0.000068	4,414	99.75	0.000514	584
70.00	0.000109	2,749	99.90	0.000602	498
80.00	0.000159	1,889			

ESTIMATED PERCENTILE OF PER-CAPITA DAYS LESS THAN/EQUAL TO CALCULATED EXPOSURE
in mg/kg body-wt/day and corresponding Margin of Exposure (MOE)

PERCENTILE	EXPOSURE	MOE 2/	PERCENTILE	EXPOSURE	MOE
10.00	0.000018	16,935	90.00	0.000225	1,336
20.00	0.000023	13,016	95.00	0.000280	1,073
30.00	0.000030	10,146	97.50	0.000332	902
40.00	0.000037	8,089	99.00	0.000402	747
50.00	0.000049	6,158	99.50	0.000459	654
60.00	0.000068	4,414	99.75	0.000514	584
70.00	0.000109	2,750	99.90	0.000602	498
80.00	0.000159	1,890			

ACUTE EXPOSURE (EX4) ANALYSIS FOR METHIDATHION
Residue file name: METHATAG Analysis date: 06-15-2000
1989-92 DATA Adjustment factor #2 NOT used
DPR NOEL (Acute) = 0.300000 mg/kg body-wt/day

CUSTOM DEMOGRAPHICS 1: Workers, 16+ yrs
All Seasons
All Regions
Sex: M/F-all/
All Races
Age-Low: 16 yrs High: 110 yrs

	Daily Exposure Analysis (mg/kg body-weight/day) per Capita	per User
Mean	0.000086	0.000086
Standard Deviation	0.000107	0.000107
Standard Error	0.000001	0.000001

Percent of Person-Days that are User-Days =100.00%

ESTIMATED PERCENTILE OF USER-DAYS LESS THAN/EQUAL TO CALCULATED EXPOSURE
in mg/kg body-wt/day and corresponding Margin of Exposure (MOE)

PERCENTILE	EXPOSURE	MOE 2/	PERCENTILE	EXPOSURE	MOE
10.00	0.000016	19,043	90.00	0.000226	1,330
20.00	0.000021	14,149	95.00	0.000293	1,024
30.00	0.000027	11,316	97.50	0.000370	812
40.00	0.000033	9,107	99.00	0.000489	614
50.00	0.000041	7,229	99.50	0.000599	501
60.00	0.000055	5,472	99.75	0.000723	415
70.00	0.000080	3,729	99.90	0.000889	337
80.00	0.000142	2,113			

ESTIMATED PERCENTILE OF PER-CAPITA DAYS LESS THAN/EQUAL TO CALCULATED EXPOSURE
in mg/kg body-wt/day and corresponding Margin of Exposure (MOE)

PERCENTILE	EXPOSURE	MOE 2/	PERCENTILE	EXPOSURE	MOE
10.00	0.000016	19,051	90.00	0.000226	1,330
20.00	0.000021	14,150	95.00	0.000293	1,024
30.00	0.000027	11,317	97.50	0.000370	812
40.00	0.000033	9,108	99.00	0.000489	614
50.00	0.000041	7,230	99.50	0.000599	501
60.00	0.000055	5,472	99.75	0.000723	415
70.00	0.000080	3,729	99.90	0.000889	337
80.00	0.000142	2,113			

Chronic Exposure (EX1) Analysis for Methidathion
RESIDUE FILE NAME: METHCTAG ANALYSIS DATE: 06-14-2000
NFCS Combined 89-92 DATA
EPA Reference dose (RfD, chronic) = 0.001500 mg/kg body-wt/day
DPR NOEL (Chronic) = 0.150000 mg/kg body-wt/day
COMMENT 1: Aggregate Dietary (Tier 4) and Drinking Water Exposure

RESIDUE FILE LISTING

TAS CODE	CROP GRP	FOOD NAME	RESIDUE (PPM)	ADJ. FCTRS #1	ADJ. FCTRS #2	SOURCE CODE
20	K	CITRUS CITRON	0.001820	25.00	1.00	PDP-OR
22	K	GRAPEFRUIT-PEELED FRUIT	0.011000	0.10	1.00	DPR
23	K	GRAPEFRUIT-JUICE	0.011000	0.10	1.00	DPR
24	K	KUMQUATS	0.005000	1.00	1.00	DPR
26	K	LEMONS-PEELED FRUIT	0.007000	0.10	1.00	DPR
27	K	LEMONS-PEEL	0.007000	2.50	1.00	DPR
28	K	LEMONS-JUICE	0.007000	0.10	1.00	DPR
30	K	LIMES-PEELED FRUIT	0.006000	0.10	1.00	DPR
31	K	LIMES-PEEL	0.006000	2.50	1.00	DPR
32	K	LIMES-JUICE	0.006000	0.10	1.00	DPR
33	K	ORANGES-JUICE-CONCENTRATE	0.000350	1.00	1.00	PDP
34	K	ORANGES-PEELED FRUIT	0.000618	1.00	1.00	PDP95%
35	K	ORANGES-PEEL	0.000618	25.00	1.00	PDP95%
36	K	ORANGES-JUICE	0.000350	1.00	1.00	PDP
37	K	TANGELOS	0.005000	0.10	1.00	DPR
38	K	TANGERINES	0.015000	0.10	1.00	DPR
39	K	TANGERINES-JUICE	0.015000	0.10	1.00	DPR
40	R	ALMONDS	0.025000	1.00	0.15	1/2TOL
41	R	BRAZIL NUTS	0.025000	1.00	1.00	1/2TOL
42	R	CASHEWS	0.025000	1.00	1.00	1/2TOL
43	R	CHESTNUTS	0.025000	1.00	1.00	1/2TOL
44	R	FILBERTS (HAZELNUTS)	0.025000	1.00	1.00	1/2TOL
45	R	HICKORY NUTS	0.025000	1.00	1.00	1/2TOL
46	R	MACADAMIA NUTS (BUSH NUTS)	0.025000	1.00	1.00	1/2TOL
47	R	PECANS	0.025000	1.00	1.00	1/2TOL
48	R	WALNUTS	0.025000	1.00	0.10	1/2TOL
49	R	BUTTER NUTS	0.025000	1.00	1.00	1/2TOL
50	A	PISTACHIO NUTS	0.025000	1.00	1.00	1/2TOL
51	R	BEECHNUTS	0.025000	1.00	1.00	1/2TOL
52	L	APPLES	0.005000	1.00	0.15	PDP
53	L	APPLES-DRIED	0.005000	8.00	0.15	PDP
54	L	APPLES-JUICE/CIDER	0.001500	1.30	0.15	PDP
55	L	CRABAPPLES	0.005000	1.00	0.15	PDP-AP
56	L	PEARS	0.005000	1.00	0.10	PDP
57	L	PEARS-DRIED	0.005000	6.25	0.10	PDP
58	L	QUINCES	0.005000	1.00	1.00	DPR
59	M	APRICOTS	0.005000	1.00	1.00	DPR
60	M	APRICOTS-DRIED	0.005000	6.00	1.00	DPR
61	M	CHERRIES	0.005000	1.00	1.00	DPR

TAS CODE	CROP GRP	FOOD NAME	RESIDUE (PPM)	ADJ. FCTRS #1	ADJ. FCTRS #2	SOURCE CODE
62	M	CHERRIES-DRIED	0.005000	4.00	1.00	DPR
63	M	CHERRIES-JUICE	0.005000	1.50	1.00	DPR
64	M	NECTARINES	0.005000	1.00	0.35	DPR
65	M	PEACHES	0.001500	1.00	0.35	PDP
66	M	PEACHES-DRIED	0.001500	7.00	0.35	PDP
67	M	PLUMS(DAMSONS)	0.005000	1.00	1.00	DPR
68	M	PLUMS-PRUNES(DRIED)	0.005000	5.00	1.00	DPR
69	M	PLUMS/PRUNE-JUICE	0.005000	1.40	1.00	DPR
80	A	MANGOES	0.025000	1.00	1.00	1/2TOL
82	A	OLIVES	0.025000	1.00	0.10	1/2TOL
97	A	KIWI FRUIT	0.005000	1.00	0.15	DPR
103	A	SUGAR APPLES (SWEETSOP)	0.100000	1.00	1.00	1/2TOL
106	A	CARAMBOLA (STARFRUIT)	0.050000	1.00	1.00	1/2TOL
108	A	LONGAN FRUIT	0.050000	1.00	1.00	1/2TOL
181	A	ARTICHOKES-GLOBE	0.005000	1.00	1.00	DPR
203	B	ARTICHOKES-JERUSALEM	0.005000	1.00	1.00	DPR
246	A	SUNFLOWER-SEEDS-WITH HULLS	0.250000	1.00	1.00	1/2TOL
275	O	SORGHUM (INCLUDING MILO)	0.100000	1.00	1.00	1/2TOL
290	A	COTTONSEED-OIL	0.100000	1.00	0.01	1/2TOL
291	A	COTTONSEED-MEAL	0.100000	1.00	0.01	1/2TOL
294	A	SAFFLOWER-SEED	0.250000	1.00	1.00	1/2TOL
295	A	SAFFLOWER-OIL	0.250000	1.00	1.00	1/2TOL
298	A	SUNFLOWER-OIL	0.250000	1.00	1.00	1/2TOL
300	A	OLIVE OIL	0.025000	1.00	0.10	1/2TOL
377	L	APPLES-JUICE-CONCENTRATE	0.001500	3.90	0.15	PDP
402	M	PEACHES-JUICE	0.001500	1.00	0.35	PDP
404	L	PEARS-NECTAR	0.005000	1.00	0.10	PDP
410	M	APRICOT JUICE OR NECTAR	0.005000	1.00	1.00	DPR
417	A	SUNFLOWER-SEEDS-HULLED	0.250000	1.00	1.00	1/2TOL
420	K	TANGERINES-JUICE-CONCENTRATE	0.015000	0.32	1.00	DPR
431	R	WALNUT OIL	0.025000	1.00	0.10	1/2TOL
432	A	WATER-BOTTLED	0.000029	1.00	1.00	
433	A	WATER-TAP	0.000029	1.00	1.00	
434	A	WATER-COMMERCIAL PROCESSING	0.000029	1.00	1.00	
435	A	WATER-NON-FOOD BASED	0.000029	1.00	1.00	
441	K	GRAPEFRUIT-JUICE-CONCENTRATE	0.011000	0.39	1.00	DPR
442	K	LEMONS-JUICE-CONCENTRATE	0.007000	0.57	1.00	DPR
443	K	LIMES-JUICE-CONCENTRATE	0.006000	0.30	1.00	DPR
448	K	GRAPEFRUIT PEEL	0.014000	2.50	1.00	DPR

Chronic Exposure (EX1) Analysis for Methidathion
RESIDUE FILE NAME: METHCTAG ANALYSIS DATE: 06-14-2000
NFCS Combined 89-92 DATA
EPA Reference dose (RfD, chronic) = 0.001500 mg/kg body-wt/day
DPR NOEL (Chronic) = 0.150000 mg/kg body-wt/day
COMMENT 1: Aggregate Dietary (Tier 4) and Drinking Water Exposure

TOTAL EXPOSURE BY POPULATION SUBGROUP

POPULATION SUBGROUP	TOTAL EXPOSURE mg/kg body-wt/day	Margin of Exposure 1/	Percent of RfD
U.S. POP - 48 STATES - ALL SEASONS	0.000004	41,721	0.2%
U.S. POPULATION - SPRING SEASON	0.000003	42,891	0.2%
U.S. POPULATION - SUMMER SEASON	0.000004	38,645	0.3%
U.S. POPULATION - AUTUMN SEASON	0.000003	43,609	0.2%
U.S. POPULATION - WINTER SEASON	0.000004	42,340	0.2%
NORTHEAST REGION	0.000004	41,680	0.2%
MIDWEST REGION	0.000003	43,227	0.2%
SOUTHERN REGION	0.000003	44,282	0.2%
WESTERN REGION	0.000004	36,899	0.3%
PACIFIC REGION	0.000004	36,967	0.3%
HISPANICS	0.000004	41,259	0.2%
NON-HISPANIC WHITES	0.000004	42,045	0.2%
NON-HISPANIC BLACKS	0.000003	43,658	0.2%
NON-HISPANIC OTHER THAN BLACK OR WHITE	0.000005	29,609	0.3%
ALL INFANTS	0.000011	13,941	0.7%
NURSING INFANTS (<1 YEAR OLD)	0.000003	46,220	0.2%
NON-NURSING INFANTS (<1 YEAR OLD)	0.000014	10,861	0.9%
CHILDREN (1-6 YEARS)	0.000007	20,286	0.5%
CHILDREN (7-12 YEARS)	0.000005	27,917	0.4%
FEMALES (13-19 YRS/NOT PREG. OR NURSING)	0.000002	67,604	0.1%
FEMALES (20+ YEARS/NOT PREG. OR NURSING)	0.000003	52,260	0.2%
FEMALES (13-50 YEARS)	0.000003	55,059	0.2%
FEMALES (13+/PREGNANT/NOT NURSING)	0.000004	39,644	0.3%
FEMALES (13+/NURSING)	0.000006	24,061	0.4%
MALES (13-19 YEARS)	0.000003	52,174	0.2%
MALES (20+ YEARS)	0.000003	53,339	0.2%
SENIORS (55+)	0.000003	49,263	0.2%

1. Margin of Exposure = DPR NOEL / Dietary Exposure

Chronic Exposure (EX1) Analysis for Methidathion
RESIDUE FILE NAME: METHCTAG ANALYSIS DATE: 06-21-2000
NFCS Combined 89-92 DATA
Q_1 = 0.340000
COMMENT 1: Aggregate Dietary (Tier 4) and Drinking Water Exposure

TOTAL EXPOSURE BY POPULATION SUBGROUP

POPULATION SUBGROUP	TOTAL EXPOSURE mg/kg body-wt/day	TOTAL EXPOSURE Life-Time Risk (Q_1=0.340000)
U.S. POP - 48 STATES - ALL SEASONS	0.000004	1.22E-06
U.S. POPULATION - SPRING SEASON	0.000003	1.19E-06
U.S. POPULATION - SUMMER SEASON	0.000004	1.32E-06
U.S. POPULATION - AUTUMN SEASON	0.000003	1.17E-06
U.S. POPULATION - WINTER SEASON	0.000004	1.20E-06
NORTHEAST REGION	0.000004	1.22E-06
MIDWEST REGION	0.000003	1.18E-06
SOUTHERN REGION	0.000003	1.15E-06
WESTERN REGION	0.000004	1.38E-06
PACIFIC REGION	0.000004	1.38E-06
HISPANICS	0.000004	1.24E-06
NON-HISPANIC WHITES	0.000004	1.21E-06
NON-HISPANIC BLACKS	0.000003	1.17E-06
NON-HISPANIC OTHER THAN BLACK OR WHITE	0.000005	1.72E-06
ALL INFANTS	0.000011	3.66E-06
NURSING INFANTS (<1 YEAR OLD)	0.000003	1.10E-06
NON-NURSING INFANTS (<1 YEAR OLD)	0.000014	4.70E-06
CHILDREN (1-6 YEARS)	0.000007	2.51E-06
CHILDREN (7-12 YEARS)	0.000005	1.83E-06
FEMALES (13-19 YRS/NOT PREG. OR NURSING)	0.000002	7.54E-07
FEMALES (20+ YEARS/NOT PREG. OR NURSING)	0.000003	9.76E-07
FEMALES (13-50 YEARS)	0.000003	9.26E-07
FEMALES (13+/PREGNANT/NOT NURSING)	0.000004	1.29E-06
FEMALES (13+/NURSING)	0.000006	2.12E-06
MALES (13-19 YEARS)	0.000003	9.77E-07
MALES (20+ YEARS)	0.000003	9.56E-07
SENIORS (55+)	0.000003	1.04E-06

Chronic Exposure (EX1) Analysis for Methidathion
RESIDUE FILE NAME: METHCTAG ANALYSIS DATE: 06-21-2000
NFCS Combined 89-92 DATA
Q_1* = 0.530000
COMMENT 1: Aggregate Dietary (Tier 4) and Drinking Water Exposure

TOTAL EXPOSURE BY POPULATION SUBGROUP

POPULATION SUBGROUP	TOTAL EXPOSURE mg/kg body-wt/day	TOTAL EXPOSURE Life-Time Risk (Q_1*=0.530000)
U.S. POP - 48 STATES - ALL SEASONS	0.000004	1.91E-06
U.S. POPULATION - SPRING SEASON	0.000003	1.85E-06
U.S. POPULATION - SUMMER SEASON	0.000004	2.06E-06
U.S. POPULATION - AUTUMN SEASON	0.000003	1.82E-06
U.S. POPULATION - WINTER SEASON	0.000004	1.88E-06
NORTHEAST REGION	0.000004	1.91E-06
MIDWEST REGION	0.000003	1.84E-06
SOUTHERN REGION	0.000003	1.80E-06
WESTERN REGION	0.000004	2.15E-06
PACIFIC REGION	0.000004	2.15E-06
HISPANICS	0.000004	1.93E-06
NON-HISPANIC WHITES	0.000004	1.89E-06
NON-HISPANIC BLACKS	0.000003	1.82E-06
NON-HISPANIC OTHER THAN BLACK OR WHITE	0.000005	2.69E-06
ALL INFANTS	0.000011	5.70E-06
NURSING INFANTS (<1 YEAR OLD)	0.000003	1.72E-06
NON-NURSING INFANTS (<1 YEAR OLD)	0.000014	7.32E-06
CHILDREN (1-6 YEARS)	0.000007	3.92E-06
CHILDREN (7-12 YEARS)	0.000005	2.85E-06
FEMALES (13-19 YRS/NOT PREG. OR NURSING)	0.000002	1.18E-06
FEMALES (20+ YEARS/NOT PREG. OR NURSING)	0.000003	1.52E-06
FEMALES (13-50 YEARS)	0.000003	1.44E-06
FEMALES (13+/PREGNANT/NOT NURSING)	0.000004	2.01E-06
FEMALES (13+/NURSING)	0.000006	3.30E-06
MALES (13-19 YEARS)	0.000003	1.52E-06
MALES (20+ YEARS)	0.000003	1.49E-06
SENIORS (55+)	0.000003	1.61E-06